

16:13:14

OCA PAD AMENDMENT - PROJECT HEADER INFORMATION

05/19/93

Active

Project #: E-19-685                      Cost share #:                      Rev #: 2  
 Center #: 10/24-6-R7106-2A0      Center shr #:                      OCA file #:  
 Contract #: 5 R01 HL45485-02                      Mod #: MEMO OF 3/30/93      Work type : RES  
 Prime #:                      Document : GRANT  
    Contract entity: GTRC

Subprojects ? : N    CFDA:  
 Main project #:    PE #: N/A

Project unit:    CHEM ENGR                      Unit code: 02.010.114  
 Project director(s):  
 YOGANATHAN A P    CHEM ENGR                      (404)894-2849

Sponsor/division names: DHHS/PHS/NIH                      / NATL INSTITUTES OF HEALTH  
 Sponsor/division codes: 108    / 001

Award period:                      920101                      to                      921231 (performance)                      930331 (reports)

Sponsor amount	New this change	Total to date
Contract value	(1,298.34)	134,111.66
Funded	(1,298.34)	134,111.66
Cost sharing amount		0.00

Does subcontracting plan apply ? : N

Title: QUANTITATION OF VALVULAR REGURGITATION: AN IN VITRO STUDY

PROJECT ADMINISTRATION DATA

OCA contact: Kathleen R. Ehlinger                      894-4820

Sponsor technical contact

Sponsor issuing office

DR. MIRILEE PEARL  
(301)496-1081

J. KEVIN KEATING  
(301)496-7536

NATIONAL INSTITUTES OF HEALTH  
NHLB INSTITUTE  
CARDIAC DISEASES BRANCH  
FEDERAL BUILDING, ROOM 3C06  
BETHESDA, MD 20893

NATIONAL INSTITUTES OF HEALTH  
NHLB INSTITUTE  
GRANTS OPERATION BRANCH  
FEDERAL BUILDING  
BETHESDA, MD. 20893

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

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

Administrative comments -

ISSUED TO REDUCE PROJECT BY \$1,298.34. CARRY FORWARD UNEXPENDED FUNDS TO CONTINUATION E-19-X13.

Project # E-19-685 Center # 10/24-6-R7106-2A0  
 Project Director YOGANATHAN A P Unit 02.010.114  
 Contract/Grant # 5 RO1 HL45485-02 Contract Entity GTRC  
 Sponsor 108 001 Prime Contract #

DHHS/PHS/NIH/NATL INSTITUTES OF H  
 Title Closeout Initiation Complete Date 930729 Project Status T

QUANTITATION OF VALVULAR REGURGITATION: AN IN VITRO STUDY

Award Period: 920101 to 921231

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	

Comment CONTINUED BY E-19-X13.

F8 Next

F12 Return

Georgia Institute of Technology  
Hinman Building  
Atlanta, Georgia 30332-0259  
USA  
404•894•4624; 2629  
Fax: 404•894•5519

April 5, 1993

To: Dr. A. P. Yoganathan, Chemical Engineering  
From: David Welch, Director  
Subject: Issuance of Financial Status Report

Attached is the hard copy of the Financial Status Report for project E-19-685 which was electronically transmitted to NIH on 3/31/93. The figures reported have been verified with Claudia Clarkson.

Please note that a carryforward request of \$1,298.34 has been included in the Remarks section. Also, since the carryforward requested from project E-19-606 in the amount of \$1,192.06 was not budgeted into E-19-685, it too can be added to the budget for year 3 (E-19-X13). To increase the budget of the continuation project E-19-X13 you may submit a copy of this report along with a Budget Revision to Sponsored Project to OCA for the amount of the carryforward. Please be sure to include an appropriate allocation for indirect charges in the budget revision request. OCA has been notified via electronic mail that the budget has been reduced to zero.

If you have any questions about this report, please contact Sandy Mason at 4-5524.

**Attachment**

xc: Ms. Claudia Clarkson, Chemical Engineering, 0100  
Ms. K. R. Ehlinger, OCA/PAD, 0420  
Ms. D. Herrmann, OCA/CSD, 0420  
File 246R71062A0

RECEIVED

APR 08 1993

OFFICE OF CONTRACT  
AND ADMINISTRATION

## ELECTRONICALLY TRANSMITTED FINANCIAL STATUS REPORT

1. NIH  
Recipient Org GEORGIA INSTITUTE OF TECHNOLOGY

2. GRANT ID 5 R01 HL45485-02  
4. ID 1580603146A1

5. Recipient ID E-19-685

8. Project Period 01-01-91 / 12-31-94

9. Report Period 01-01-92 / 12-31-92

10.

a. Net Outlays previously reported	136,881.94	(10A)
b. Total Outlays this report period	132,032.74	(10B)
c. Less:Program Income Credits	0.00	(10C)
d. Net outlays this report period	132,032.74	(10D)
e. Net outlays to date	268,914.68	(10E)
f. Less:Non-Federal share of outlays	0.00	(10F)
g. Total Federal share of outlays	268,914.68	(10G)
h. Total unliquidated obligations	2,078.92	(10H)
i. Less:Non-Federal share of unliquidated obligations	0.00	(10I)
j. Federal share of unliquidated obligations	2,078.92	(10J)
k. Total Federal Share - outlays & unliquidated obligations	270,993.60	(10K)
l. Total cumulative amount of Federal funds authorized	273,484.00	(10L)
m. Unobligated balance of Federal funds	2,490.40	(10M)
x. Grantee carryover request	1,298.34	(10X)
z. Previous budget period carryover request	1,192.06	(10Z)

11. Indirect Expense

Rate	Base	Subtotal	Total	Fed Share
61.50 (b)	30,188.43 (c)	18,565.89 (f)	48,386.12 (d)	48,386.12 (e)
55.20 (g)	54,022.14 (h)	29,820.23 (i)		
0.00 (j)	0.00 (k)	0.00 (l)		
0.00 (m)	0.00 (n)	0.00 (p)		
0.00 (Q)	0.00 (R)	0.00 (S)		
0.00 (T)	0.00 (U)	0.00 (V)		

REMARKS: ANY QUESTIONS PERTAINING TO THIS REPORT SHOULD BE DIRECTED  
TO SANDY MASON AT (404) 894-5524.  
CARRYFORWARD REQUEST \$1,298.34

13a. Authorized Official DAVID V. WELCH, DIRECTOR c. Date 03-31-93  
b. Title GRANTS & CONTRACTS ACCOUNTING d. Phone 404-894-2629

RCVD: 04-01-93 ACCEPTED 04-01-93

ENTER DOCUMENT NUMBER (e.g. R1AI12345A) OR  
GRANT NUMBER (e.g. 1R01AI12345-01A1) OR  
END

<b>PROGRESS REPORT SUMMARY</b>		<b>GRANT NUMBER</b>	
		HL 45485-03	
<b>PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR</b>		<b>PERIOD COVERED BY THIS REPORT</b>	
Ajit P. Yoganathan		<b>FROM</b>	<b>THROUGH</b>
<b>APPLICANT ORGANIZATION</b>			
Georgia Institute of Technology		01/01/92	12/31/92
<b>TITLE OF PROJECT (Repeat title shown in item 1 on first page)</b>			
Quantitation of Valvular Regurgitation: An In Vitro Study			
(SEE INSTRUCTIONS)			

**1. Specific Aims**

The goals of this proposal are three-fold. **First**, the study will address the hypothesis that equations can be derived from basic fluid mechanic principles to quantify regurgitant volume using quantities that can be directly measured by Doppler. **Second**, these basic physical principles can be used to interpret color flow mapping variability related to regurgitant jet behavior in the presence of solid structures or interrupting flows. **Third**, additional variability inherent to measurement technique (i.e. instrument settings) will be addressed.

To achieve these objectives, the following specific aims are proposed: 1) to derive equations from the principles of turbulent jet flow and conservation of mass which provide orifice flow rate, and therefore regurgitant volume, as a function of Doppler measurable quantities; 2) in *in vitro* models, to test the accuracy of the equations in predicting actual regurgitant volume; 3) to define in an *in vitro* model, the relationship between regurgitant flow, and spatial characteristics of the color flow jet, namely, jet length, width, area, and volume; 4) in *in vitro* models, to address the variability in these relationships due to machine settings, driving pressure, and physiologically observed jet flow phenomena, namely, the Coanda effect, impingement, counterflow, and coflow; and 5) to investigate the applicability of the quantitation techniques to various designs of heart valve prostheses.

These comprehensive studies are performed *in vitro* in order to allow precise and independent control of all variables. *In vivo* studies, while providing realistic environments, do not generally allow independent control of variables such as is required for such fundamental studies. Careful design of flow models provides semi-realistic environments, while allowing dependent control.

**2. Studies and Results**

**A. CONSERVATION OF MOMENTUM TECHNIQUE APPLIED TO REGURGITANT JETS**

The purpose of this study was to determine whether the inverse relationship of centerline velocity to distance develops sufficiently rapidly so that quantitative techniques based on that decay would be applicable over a wide range of heart rates. Two different techniques, an engineering tool, laser Doppler anemometry, and a clinical tool, Doppler ultrasound, were used for measuring jet centerline velocities (averaged over multiple beats). Physiologic pulsatile flows were pumped through two circular orifices, 4 and 6 mm in diameter, at 60 to 150 beats/min; peak orifice velocities ranged from 2 to 5 m/sec. Steady flow experiments were also performed with the same orifice diameters and over the same velocity range. Peak centerline velocities in the fully developed turbulent jet region decayed inversely with distance at all heart rates studies. With laser

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Doppler anemometry, the proportionality constant of the decay curve was found to be in the range  $6.4 \pm 0.5$ . The pulsed Doppler results provided a jet constant in the range  $6.7 \pm 0.3$  with the 4-mm orifice diameter, whereas the constant was  $6.5 \pm 0.3$  with the 6-mm orifice diameter. In steady flow, the proportionality constant was found to be  $6.1 \pm 0.2$ . Therefore, within a wide range of physiologic heart rates, full jet development occurs with sufficient speed so that the expected centerline velocity decay is established (jet empirical constant of 6.3). The conservation of momentum technique for calculating orifice flow rate on the basis of these centerline velocities is thus applicable under physiologic conditions.

### B. EFFECT OF COUNTER AND CO-FLOWS ON REGURGITANT JETS

The purpose of this study was to address the hypothesis that physiologic counterflow field may influence regurgitant jet size. Steady flow was driven through 0.02-.12 cm<sup>2</sup> circular orifices at .5-5 m/s. At a constant orifice velocity and flow rate, the velocity of a uniform counterflow field was varied from 1 to 8 cm/s. Jet penetration length was measured by fluorescent dye visualization in 10 videoframes to average out turbulent fluctuations. Despite its relatively low velocities, counterflow dramatically curtailed jet length. For example, the length of a 1.8 m/s jet (.05 cm<sup>2</sup> orifice) decreased from 20 to 10 cm as counterflow velocity increased from 3 to 7.5 cm/s. Jet length decreased as the ratio of counterflow to jet momentum increased, but with a nonlinear relationship: length declined steeply for low-momentum jets (momentum ratio < 1.0) and with a more shallow slope for high-momentum jets (ratio > 1.0). Counterflow fields analogous to atrial inflow have an important effect on the length of regurgitant jets. Low-momentum jets, such as TR, are more sensitive to counterflow, while high-momentum jets, such as significant MR, are less sensitive. Further studies have also shown that wall jets in a counterflow are uniformly longer than center jets (up to 40% longer for jets of high momentum).

### C. PROXIMAL FLOW CONVERGENCE STUDIES

Recent studies have shown that the flow convergence region proximal to an orifice can be used to quantify flow rate by Doppler flow mapping. Clinically, however, flow may converge toward aortic or mitral regurgitant orifices over a 3-dimensional (3D) or conical angle. Therefore, we tested the hypothesis that calculating orifice flow rate requires that the 3D angle of approach be taken into account. Steady flow (1-3 l/min) was pumped through circular orifices in an upright and inverted 90° cone and flow rate was calculated with and without the 3D angle factor. Flow rates calculated assuming a hemispherical convergence region underestimated actual values by  $46 \pm 4\%$  for the upright cone and overestimated them by  $230 \pm 26\%$  for the inverted cone. Correcting for the 3D angle gave values within 5% of actual ones ( $r=.98$ ,  $SEE=.13$  l/min). Application of the proximal convergence method for flow through restrictive orifices must take into account the three-dimensional angle determined by the surrounding leaflets.

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Georgia Institute of Technology			
TITLE OF PROJECT (Repeat title shown in item 1 on first page)			
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(SEE INSTRUCTIONS)			

#### D. CONFINED AND IMPINGING JETS

The distal jet centerline velocity technique, previously described was tested on pure confined, pure impinging and confined impinging jets. When the distance between the orifice and the impinging wall becomes relatively small, in addition to the confinement created by the side walls, it may be hypothesized that the jet momentum is no longer conserved. Physiologic pulsatile flow as pumped through circular orifices (2-4 mm) at 70-150 beats/min in two receiving chambers (51 and 88 mm in diameter); at each heart rate, peak velocity was varied from 2-5 m/s, and the orifice-to-end wall spacing was varied from 30-93 mm. Centerline velocities were recorded by echo Doppler, averaged over multiple beats over a wide physiologic range of heart rates, and sufficient distance from the back wall, full jet development occurs with sufficient speed so that the expected centerline velocity decay curve is established at peak flow. The conservation of momentum technique for calculating orifice flow rate based on these centerline velocities should therefore be applicable at reasonable orifice-to-end wall spacings.

#### E. COMPUTER SIMULATION STUDIES

Despite a series of studies showing variability in color Doppler jet areas (CJA) due to factors other than regurgitant flow rate, such measurements are still the best available non-invasive markers of the severity of regurgitation in the clinical setting. To rigorously explore factors affecting jet size, a computer model was developed which simulates color Doppler jets for relevant physiologic and technical inputs. The computer model allows rigorous testing of factors affecting jet size to an extent not available *in vitro* or *in vivo*. Such detailed studies will aid new experimental designs and potentially lead to new quantitation techniques.

### 3. Significance

During the past year we have continued to validate that fundamental engineering (fluid mechanic) principals can be applied to study and quantitate valvular regurgitation. The results of our studies will be valuable to cardiologists as they attempt to use echo Doppler techniques to non-invasively quantitate valvular regurgitation in their patients.

The free jet studies clearly demonstrated that the conservation of momentum technique is applicable to regurgitant jets that occur *in vivo*. The counterflow work showed that the jet length and area measurements currently used in clinical practice are flawed and could lead to erroneous interpretation of the severity of tricuspid and mitral regurgitation.

The computer model demonstrated the value of computer simulation studies in reducing the need for costly and time consuming *in vitro* and *in vivo* experimental/clinical studies.

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APPLICANT ORGANIZATION Georgia Institute of Technology		FROM 01/01/92	THROUGH 12/31/92
TITLE OF PROJECT (Repeat title shown in Item 1 on first page) Quantitation of Valvular Regurgitation: An In Vitro Study (SEE INSTRUCTIONS)			

#### 4. Plans

No changes to plans originally purposed.

- (i) Detailed pulsatile flow studies will be conducted on central and wall jets in counter and co-flowing environments.
- (ii) Pulsatile flow studies to test the validity of the proximal flow convergence technique to quantitate regurgitant volume.
- (iii) Begin studies to investigate the effects of receiving chamber compliance.
- (iv) Conduct steady flow studies on prosthetic heart valves, to study the applicability of the distal jet and proximal flow convergence techniques, to quantitate prosthetic valve regurgitation.
- (v) Write journal articles based on the results of the studies conducted during the first two years of the project.

#### 5. Human Subjects

N/A

#### 6. Vertebrate Animals

N/A

#### 7. Publications

##### A. Manuscripts

1. Parro, A., Philpot, E. F., Nanda, N. C., Cape, E. G., and Yoganathan, A. P., "Amplitude Information from Color Doppler: A Preliminary Study of the Power Mode," *Journal of the American College of Cardiology*, vol 18, pp. 997-1003, 1991.
2. Cape, E. G., Jaarsma, W., and Yoganathan, A. P., "Echo Doppler Principles, Techniques and Applications for the Cardiac Surgeon," *European Journal of Cardiothoracic Surgery*, vol. 6, (supplement 1) pp. S2-S12, 1992.
3. Cagniot, A., Cape, E. G., Levine, R. A., Walker, P. G., and Yoganathan, A. P., "Effect of Heart Rate on Center-line Velocities of Pulsatile Intracardiac Jets: An In Vitro Study Using Laser Doppler Anemometry and Pulsed Doppler Ultrasound," *Journal of the American Society of Echocardiography*, vol. 5, pp. 393-404, 1992.



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Quantitation of Valvular Regurgitation: An In Vitro Study (SEE INSTRUCTIONS)			

4. Cape, E. G., Levine, R. A., and Yoganathan, A. P., "Heart Rate/Frame Rate Interaction in Color Doppler Flow Mapping of Pulsatile Turbulent Jets: *In Vitro* Studies," *Journal of the American College of Cardiology*. (In Press)
5. Grimes, R., Levine, R. A., Walker, P. G., and Yoganathan, A. P., "The Effects of Atrial Inflow on Regurgitant Jets: *In Vitro* studies," *Journal of the American College of Cardiology*. (Submitted)

**B. Abstracts and Conference Presentations**

1. Cape, E. G., Nanda, N. C. and Yoganathan, A. P., "Doppler Assessment of Regurgitant Flow Through Bileaflet Heart Valve Prostheses: Pulsatile *In Vitro* Studies," 64th Annual Scientific Sessions - American Heart Association, *Circulation*, **84**, pp. II-636, 1991.
2. Weintraub, R., Shandes, R., Cranney, G., Walker, P., Yoganathan, A. and Sahn, D. J., "Comparison of Flow Convergence Calculations Using Color Doppler Flow Mapping and Phase Velocity Encoded MRI: An *In Vitro* Study," 64th Annual Scientific Sessions - American Heart Association, *Circulation*, **84**, pp. II-636, 1991.
3. Cape, E. G., Yoganathan, A. P., Thomas, J. D., and Levine, R. A., "The Effect of Leaflet Geometry on Proximal Convergence Calculations of Flow by Color Doppler," AIUM Annual Meeting, *Journal of Ultrasound in Medicine*, **11:S21**, March 1992.
4. Grimes, R., Levine, R. A., Walker, P. G., and Yoganathan, A. P., "Atrial Inflow Influences Regurgitant Jet Size," Annual Scientific Sessions - American College of Cardiology, *JACC*, vol. **19**, pp. 158A, 1992.
5. Cagniot, A., Cape, E. G., Levine, R. A., and Yoganathan, A. P., "Non Invasive Quantification of Regurgitation by Conservation of Momentum: Can it be Applied at Rapid Heart Rate?" Annual Scientific Sessions - American College of Cardiology, *JACC*, vol. **19**, pp. 357A, 1992.
6. Cape, E. G., Levine, R. A., and Yoganathan, A. P., "Computer Simulation of Color Doppler Jet Boundaries," Annual Scientific Sessions - American College of Cardiology, *JACC*, vol **19**, pp. 9A, 1992.
7. Levine, R. A., Thomas, J. D., Cape, E. G., Yoganathan, A. P., Weyman, A. E., "Three-Dimensional Orifice Geometry Correction is Required for Calculating Orifice Flow Rate by Proximal Convergence." Annual Scientific Sessions - American College of Cardiology, *JACC*, vol. **19**, pp. 378A, 1992.

**8. Inventions and Patents**

None

**PROGRESS REPORT (Personnel and Study Subjects)**

GRANT NUMBER

HL 45485-03

**All Personnel for the Current Budget Period  
and Any Planned Changes in Personnel for the Next Budget Period**

Use two sections. In the first section list *All Current Personnel*. In the second section list *Planned Personnel Changes*.

Name	Degree(s)	SSN	Role on Project (e.g., PI, Res. Assoc.)	Date of Birth (MM/DD/YY)	Annual % Effort
<b>CURRENT PERSONNEL</b>					
A. P. Yoganathan	Ph.D.	569-27-7875	PI	12/6/51	25
R. A. Levine	M.D.	060-46-5316	Consultant	1/29/53	7.5
A. Burleson	B.S.	255-67-3026	Grad Student	1/26/66	100
R. Grimes	M.D.	256-02-7222	Grad Student	12/27/62	100
F. Guenet	B.S.	252-81-8719	Grad Student	10/7/68	50
P. G. Walker	Ph.D.	252-751-226	Post Doc Fel	10/27/61	50
E. Muralidharan	Ph.D.	260-75-3075	Post Doc Fel	5/9/59	25
Y. H. Kim	Ph.D.	484-11-4483	Post Doc Fel	1/19/60	25
B. Chand		382-56-7920	Secretary	11/23/52	10
<b>PLANNED PERSONNEL CHANGES</b>					
Dr. E. Muralidharan has left Georgia Tech (5/92)					0
No other changes are currently planned.					

Provide the number of subjects enrolled in the study *to date* according to the following categories. (See Page 8 for definitions.)

	American Indian or Alaskan Native	Asian or Pacific Islander	Black, not of Hispanic Origin	Hispanic	White, not of Hispanic Origin	Other or Unknown	TOTAL
Female							
Male							
Unknown							
TOTAL							