Final Progress Report for Research Projects Funded by Health Research Grants

Instructions: Please complete all of the items as instructed. Do not delete instructions. Do not leave any items blank; responses must be provided for all items. If your response to an item is "None", please specify "None" as your response. "Not applicable" is not an acceptable response for any of the items. There is no limit to the length of your response to any question. Responses should be single-spaced, no smaller than 12-point type. The report **must be completed using MS Word**. Submitted reports must be Word documents; they should not be converted to pdf format. Questions? Contact Health Research Program staff at 717-783-2548.

1. **Grantee Institution: The** Pennsylvania State University

2. **Reporting Period (start and end date of grant award period):** 1/1/2009 – 12/31/2012

3. **Grant Contact Person (First Name, M.I., Last Name, Degrees):** John Anthony, MPA

4. **Grant Contact Person's Telephone Number:** 814-935-1081

5. **Grant SAP Number:** 4100047645

6. **Project Number and Title of Research Project:** 36 - Cannula Development and In Vivo Testing for Pediatric VAD Development

7. **Start and End Date of Research Project:** 7/20/2010 to 6/30/2011

8. **Name of Principal Investigator for the Research Project:** William J. Weiss, Ph.D.

9. **Research Project Expenses**.

   9(A) Please provide the amount of health research grant funds spent on this project for the entire duration of the grant, including any interest earned that was spent:

   $ 76,264

   9(B) Provide the last names (include first initial if multiple individuals with the same last name are listed) of **all** persons who worked on this research project and were supported with health research funds. Include position titles (Principal Investigator, Graduate Assistant, Post-doctoral Fellow, etc.), percent of effort on project and total health research funds expended for the position. For multiple year projects, if percent of effort varied from year to year, report in the % of Effort column the effort by year 1, 2, 3, etc. of the project (x% Yr 1; z% Yr 2-3).

Last Name	Position Title	% of Effort on Project	Cost
None			

9(C) Provide the names of **all** persons who worked on this research project, but who *were not* supported with health research funds. Include position titles (Research Assistant, Administrative Assistant, etc.) and percent of effort on project. For multiple year projects, if percent of effort varied from year to year, report in the % of Effort column the effort by year 1, 2, 3, etc. of the project (x% Yr 1; z% Yr 2-3).

Last Name	Position Title	% of Effort on Project
William J. Weiss, PhD	Howard E. Morgan Professor of Surgery and Bioengineering	16.7%
Gerson Rosenberg, PhD	C. McCollister Evarts, M.D. Professor in Artificial Organs; Professor of Surgery and Bioengineering	8.3%
Christopher A. Siedlecki, PhD	Jane A. Fetter Professor of Surgery and Professor of Bioengineering	4.2%
Elizabeth Carney, DVM	Assistant Professor, Comparative Medicine	4.2%
Rebecca Peterson	Animal Study Manager	24%
Branka Lukic, MS	Bioengineer	33%

9(D) Provide a list of **all** scientific equipment purchased as part of this research grant, a short description of the value (benefit) derived by the institution from this equipment, and the cost of the equipment.

Type of Scientific Equipment	Value Derived	Cost
None		

10. Co-funding of Research Project during Health Research Grant Award Period. Did this research project receive funding from any other source during the project period when it was supported by the health research grant?

Yes_____ No____X_____

If yes, please indicate the source and amount of other funds:

11. Leveraging of Additional Funds

11(A) As a result of the health research funds provided for this research project, were you able to apply for and/or obtain funding from other sources to continue or expand the research?

Yes___X_____ No_____

If yes, please list the applications submitted (column A), the funding agency (National Institutes of Health—NIH, or other source in column B), the month and year when the application was submitted (column C), and the amount of funds requested (column D). If you have received a notice that the grant will be funded, please indicate the amount of funds to be awarded (column E). If the grant was not funded, insert "not funded" in column E.

Do not include funding from your own institution or from CURE (tobacco settlement funds). Do not include grants submitted prior to the start date of the grant as shown in Question 2. If you list grants submitted within 1-6 months of the start date of this grant, add a statement below the table indicating how the data/results from this project were used to secure that grant.

A. Title of research project on grant application	B. Funding agency (check those that apply)	C. Month and Year Submitted	D. Amount of funds requested:	E. Amount of funds to be awarded:
Novel Cannulae System for Pediatric Ventricular Assist Devices	X NIH ☐ Other federal (specify:_____) ☐ Nonfederal source (specify:_)	12/5/10	$1,572,918	$ 0
Pre-clinical Testing of a VAD for Uni- and Bi-ventricular Support in Infants	X NIH ☐ Other federal (specify:_____) ☐ Nonfederal source (specify:_)	11/5/11	$ 2,984,501	$746,084

11(B) Are you planning to apply for additional funding in the future to continue or expand the research?

Yes___X_____ No____ _____

If yes, please describe your plans:

We will pursue industrial partner support.

12. Future of Research Project. What are the future plans for this research project?

A related NIH SBIR grant is currently being funded (submitted April 2010, before the start date of this Health Research Grant). Upon completion of that grant, we will pursue SBIR Phase IIb funding for pre-clinical studies of the Pediatric VAD System. At the same time, we are investigating options to partner with industry.

13. **New Investigator Training and Development**. Did students participate in project supported internships or graduate or post-graduate training for at least one semester or one summer?

Yes_____ No_____X_____

If yes, how many students? Please specify in the tables below:

	Undergraduate	Masters	Pre-doc	Post-doc
Male				
Female				
Unknown				
Total				

	Undergraduate	Masters	Pre-doc	Post-doc
Hispanic				
Non-Hispanic				
Unknown				
Total				

	Undergraduate	Masters	Pre-doc	Post-doc
White				
Black				
Asian				
Other				
Unknown				
Total				

14. **Recruitment of Out-of–State Researchers**. Did you bring researchers into Pennsylvania to carry out this research project?

Yes_____ No____X_____

If yes, please list the name and degree of each researcher and his/her previous affiliation:

15. **Impact on Research Capacity and Quality**. Did the health research project enhance the quality and/or capacity of research at your institution?

Yes___X_____ No_____

If yes, describe how improvements in infrastructure, the addition of new investigators, and other resources have led to more and better research.

This project has helped Penn State Hershey capitalize on the advances made and expertise developed in the Penn State Artificial Heart Program and apply those capabilities to enable

development of much smaller devices that are needed for use in children and infants with congenital heart problems

16. Collaboration, business and community involvement.

16(A) Did the health research funds lead to collaboration with research partners outside of your institution (e.g., entire university, entire hospital system)?

Yes_____ No____X_____

If yes, please describe the collaborations:

16(B) Did the research project result in commercial development of any research products?

Yes_____ No____X_____

If yes, please describe commercial development activities that resulted from the research project:

16(C) Did the research lead to new involvement with the community?

Yes_____ No_____X_____

If yes, please describe involvement with community groups that resulted from the research project:

17. Progress in Achieving Research Goals, Objectives and Aims.

List the project goals, objectives and specific aims (as contained in the grant application's strategic plan). Summarize the progress made in achieving these goals, objectives and aims for the entire grant award period. Indicate whether or not each goal/objective/aim was achieved; if something was not achieved, note the reasons why. Describe the methods used. If changes were made to the research goals/objectives/aims, methods, design or timeline since the original grant application was submitted, please describe the changes. Provide detailed results of the project. Include evidence of the data that was generated and analyzed, and provide tables, graphs, and figures of the data. List published abstracts, poster presentations and scientific meeting presentations at the end of the summary of progress; peer-reviewed publications should be listed under item 20.

This response should be a DETAILED report of the methods and findings. It is not sufficient to state that the work was completed. Insufficient information may result in an unfavorable performance review, which may jeopardize future funding. If research findings are pending publication you must still include enough detail for the expert peer reviewers to evaluate the progress during the course of the project.

Health research grants funded under the Tobacco Settlement Act will be evaluated via a performance review by an expert panel of researchers and clinicians who will assess project work using this Final Progress Report, all project Annual Reports and the project's strategic plan. After the final performance review of each project is complete, approximately 12-16 months after the end of the grant, this Final Progress Report, as well as the Final Performance Review Report containing the comments of the expert review panel, and the grantee's written response to the Final Performance Review Report, will be posted on the CURE Web site.

There is no limit to the length of your response. Responses must be single-spaced below, no smaller than 12-point type. If you cut and paste text from a publication, be sure symbols print properly, e.g., the Greek symbol for alpha (α) and beta (ß) should not print as boxes (□) and include the appropriate citation(s). DO NOT DELETE THESE INSTRUCTIONS.

Summary of Research Completed

The objective of this research was to continue development of the Penn State Pediatric Ventricular Assist Device (PVAD), focusing on the development of a cannulae system that is suitable for clinical use. The Pediatric VAD is a blood pump sized for infants less than one year of age, with a stroke volume of approximately 12 cc.

Under this project, we completed the design and fabrication of cannulae and connectors, and performed 2 chronic animal implantations of the PVAD (described below). This important phase of development positions us to pursue funding for the final stage of development - pre-clinical testing of the complete PVAD system.

During this year, we were awarded, with Minnetronix, Inc. (St. Paul, MN), a Small Business Innovation Research grant award from the National Institutes of Health to develop a portable pneumatic driver for the PVAD. The grant funding began in July, 2011. We also submitted an R01 grant proposal to NIH in June 2010 to support pre-clinical testing of the PVAD system, which was not funded; the proposal was re-submitted in November 2011 and will be reviewed early in 2012. We also submitted an SBIR proposal to NIH to fund further PVAD cannulae development, but this grant was not funded.

Specific Aim 1. To design and fabricate cannulae for the Penn State Infant Ventricular Assist Device (VAD) for use in human infants, utilizing an innovative ePTFE graft construction to provide flexibility, kink resistance, and biocompatibility.

We have taken the proposed cannulae design, developed detailed requirements and specifications, and fabricated pump connectors and cannulae for testing. Figure 1 shows how these cannulae are to be used in a biventricular support application. Most commonly, a single left pump is used as a left ventricular assist device (LVAD). A right pump may be used alone (RVAD) or together with the left pump [biventricular support (BiVAD)]. As shown in Table 1, there are 3 different cannulae under development for all of these applications: arterial, apical, and atrial.

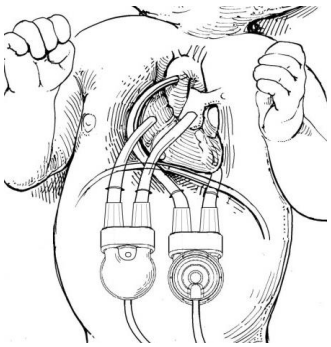

Figure 1. The Penn State Infant VAD showing application for biventricular support.

A unique aspect of our approach is the used of expanded polytetrafluoroethylene (ePTFE). ePTFE grafts are routinely used for small diameter applications (6-10 mm inner diameter), including arteriovenous conduits for vascular access in dialysis, and as femoral and popliteal artery grafts. In pediatrics, 3-6 mm ePTFE grafts are used as extra-cardiac total cavopulmonary connections, and as systemic-to-pulmonary artery shunts.

The advantages of ePTFE as a vascular graft material are related both to structure and surface chemistry. The porous microstructure consists of fibrils oriented in the axial direction (expansion direction). The pore size is defined by the fibril length, or internodal distance, which ranges from 20-90 µm. The porosity appears to support neointima formation and transmural capillary in growth.

Table 1. Cannula types to be utilized for uni- and bi-ventricular support modes.

	Inlet Cannulation		Outlet Cannulation	
	Location	Cannula Type	Location	Cannula Type
LVAD	Left ventricle apex	Apical (straight)	Ascending aorta	Arterial
	Left atrium	Atrial (curved)		
RVAD	Right atrium		Pulmonary artery	
Single ventricle (congenital anomaly)	Single ventricle apex	Apical (straight)	Ascending aorta	

The anisotropy allows tensile expansion and compression in the axial direction during bending, so that the graft can be flexed with low force, without buckling. This feature is important in the VAD application. A disadvantage of early grafts was plasma weeping resulting in perivascular seromas; however, newer constructions include hydrostatic layers. Other improvements include integral reinforcing rings (e.g. Gore Intering) and additional layers to increase suture retention, increase radial burst strength, and prevent needle hole bleeding. Chemically, ePTFE is extremely stable and resists biodegradation. It has been shown to be anti- thrombogenic and exhibits low platelet activation and inflammatory response.

We have completed 3D Solidworks models, engineering drawings, and specifications for the arterial and apical cannulae and connectors. We evaluated a number of ePTFE graft types provided by Atrium Medical Corp. We built 2 complete sets of arterial and apical cannulae, titanium connectors and apical nuts, and Delrin collets for animal testing (Figures 2 and 3). The atrial cannulae have been designed and will be completed early in 2012.

Figure 2. Pump-to-cannula connectors minimize recirculation near valves and provide a stabilized and nearly seamless interface to the ePTFE cannula.

Figure 3. Left ventricular apical connector for the inlet cannula (shown with trocar for insertion into ventricle).

Specific Aim 2. To perform two chronic animal studies of 8 week duration, to test the Infant VAD with the newly developed cannulae, by assessing thrombogenicity of the VAD/cannulae system at the extended (8 week) duration.

Methods. Briefly, the PVAD was implanted in juvenile sheep weighing 20-25 kg. The surgical approach was via a right thoracotomy. The inlet cannula was inserted into the left ventricular apex, while the outlet cannula was sewn to the descending thoracic aorta. Cardiopulmonary bypass was not used. The pump was implanted in the left preperitoneal space. The PVAD supplied approximately 2/3 of the animal's total output. All animal studies were approved by the Institutional Animal Care and Use Committee at Penn State College of Medicine. The animals were housed in facilities accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International, and veterinary care adhered to *The Guide for the Care and Use of Laboratory Animals.*

A right external jugular catheter was placed at least 2 weeks before surgery to allow platelet function to stabilize, so that the pre-operative measurements reflect normal baseline conditions. Activated partial thromboplastin time (aPTT) and antithrombin III (ATIII) were measured on a CA1500 coagulation analyzer (Dade Behring, Newark, DE) using functional clot-based assays. Heparin levels were measured on the CA1500 using a chromogenic anti-Xa assay. Thromboelastography (TEG) was used to measure the global coagulation kinetics and clot strength. Platelet aggregation was measured using whole-blood impedance platelet lumi-aggregometry (Chrono-log Whole-Blood Lumi-Aggregometer 560-CA with AGGRO/LINK® 5.1, Chrono-log Corp, Haverton, PA, USA). Activation agonists were adenosine diphosphate (ADP) (10µM) and collagen (1 µg/ml). Impedance was recorded 6 minutes after the addition of agonist.

Anticoagulation was by intravenous heparin at approximately 20 units/kg/hr, titrated to achieve a TEG R time of 2 times normal.

The Infant VAD was operated in automatic full-to-empty mode in all cases, using the air flow fill detection system. The automatic mode was set for an end-diastolic delay of 30 msecs, which was found in previous *in vitro* studies to minimize hemolysis related to inlet valve closing. The diastolic drive pressure (vacuum) was adjusted to give a mean VAD flow rate of 0.8 – 1.2 liters/min. A fixed systolic drive pressure of 250 mmHg was used and the systolic duration was adjusted as needed for complete ejection with an end-systolic delay of 10-30 msecs.

The methodology is described in Weiss et al[1] (recently accepted for publication), although the two animal studies described in this report were not included in that paper.

Results. Two animal studies were performed on March 10 and March 13, 2011.

Experiment 1. Animal # 403

This study utilized a 22.7 kg male Dorset-Finn lamb. The implantation and post-operative course were uneventful. The PVAD functioned normally. The study was electively terminated on post-operative day 35.

Figure 4 shows a portion of the hematological data. Note that the heparin levels are quite low, as the aPTT is only slightly elevated above pre-operative levels. Fibrinogen and WBC show a typical acute phase response. The plasma hemoglobin data in Figure 5 shows that hemolysis is not evident. Albumin and total protein are reduced post-operatively but return to normal.

At necropsy, the aortic anastomosis was clean and well-healed, with no grossly evident thromboemboli within the outlet cannula or the aorta to the iliac bifurcation. The inlet cannula was well-positioned in the left ventricular with no obstruction. There were no grossly evident thromboemboli within the cannula lumen. Histologically, there was variable filling of the interstitial spaces of the ePTFE with fibrin and erythrocytes. There was no fibrovascular tissue or organization present. No nuclei were observed.

A grossly observed lesion in the left kidney was consistent with a chronic cortical infarction of unknown duration. The lesion was at least 2-3 weeks old. There were microscopic lesions consistent with (but not specific for) infarction present in both kidneys. Scattered mild individual chronic glomerulosclerosis has been noted in acutely implanted lambs, consistent with a background lesion.

In summary, there was no clinical evidence of thromboembolism or end organ dysfunction during the post-operative course. The new cannulae were judged to be easy to implant, although some improvements are needed for the tools to hold the pump connectors during attachment. The necropsy results indicated excellent biocompatibility. The renal infarcts were minor, of uncertain origin, and consistent with findings in previous studies.

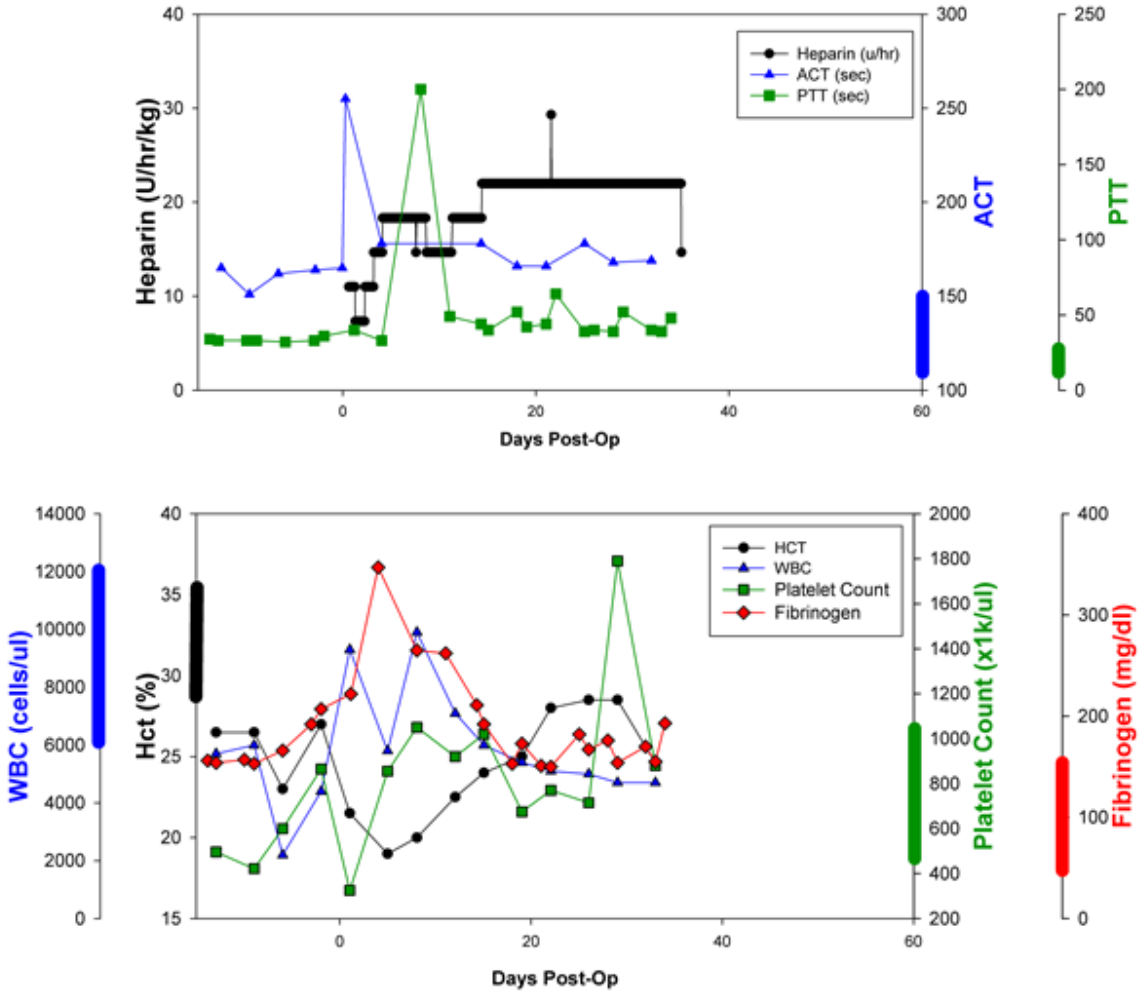

Figure 4. Hematological data for experiment #1.

<u>Experiment 2. Animal #424</u>

This study utilized a 20.5 kg male Dorset-Finn lamb. There was difficulty achieving normal tidal volumes after intubation. There was high resistance to inspiratory and expiratory flow, requiring an increase in peak inspiratory pressure. Tidal volumes gradually improved and the implantation was performed. However, respiratory function was not adequate post-operatively, and the animal was euthanized.

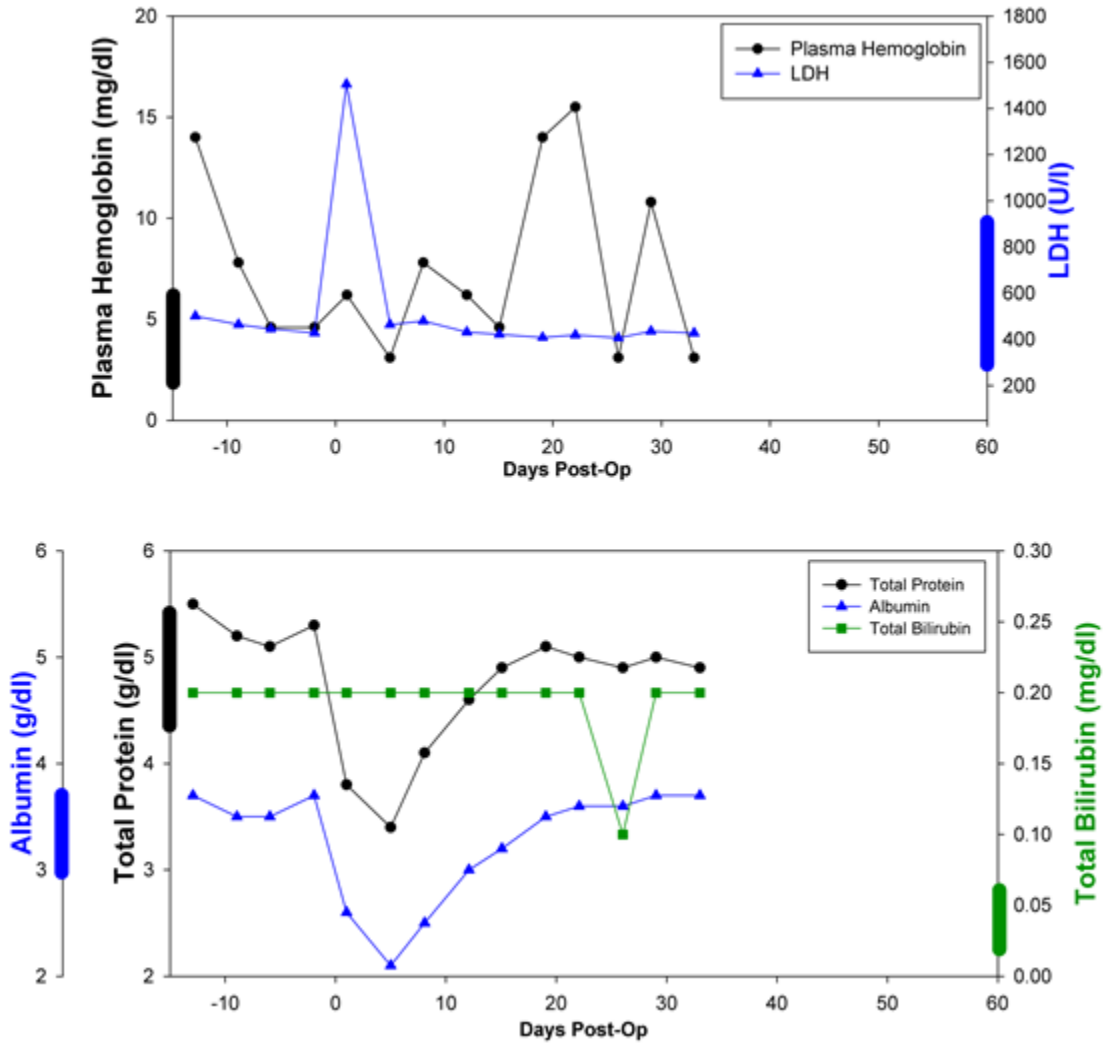

Figure 5. Plasma free hemoglobin and LDH for experiment #1 remain within normal ranges (vertical bars are +/1 standard deviation of pre-operative values pooled from all animals.)

<u>Urinary biomarkers of ischemic renal injury</u>**.** A secondary objective of this project was to improve the methods used to assess thrombogenicity in animal models. The two animal studies provided an opportunity to assess a new method for detecting renal embolization. In the ruminant animal model used for VAD testing, emboli from the VAD are more likely to travel to the kidneys or gut, rather than the brain, because the arterial cannula is anastomosed to the descending thoracic aorta in animals, rather than to the ascending aorta used in humans, and the cerebral circulation is a smaller fraction of total blood flow in animals. Furthermore, renal ischemia is clearly evident at necropsy, whereas cerebral ischemia in animals is minimized by collateral blood flow. Therefore, the documentation of renal ischemic lesions at necropsy is an important and accepted measure of thromboembolism in animal testing. However, this approach is limited, because the time of occurrence is difficult to assess accurately by histology, particularly with chronic stage lesions. It would be useful to detect renal ischemia in real time so that ischemic events could be classified, for example, as pre-operative, immediate post-operative, or late post-operative (chronic). Although repeated evaluations of serum BUN and creatinine

values are common, this is a highly insensitive measure of renal function, requiring loss of significant renal parenchyma (up to three-quarters) to see even modest increases [2].

Experimental monitoring of renal damage by evaluation of urine for secreted biomarker proteins is a well-established technique in rodents with limited clinical application in man[3-9]. When toxic or ischemic damage affects renal tubular epithelium, a number of proteins can be detected downstream in the urine with robust and exquisite sensitivity and reliability and known decay rates. We monitored the urine of lambs implanted with LVAD devices for evidence of ischemic damage by using a panel of 11 antibodies by western blotting of multiple urine samples collected before (baseline) and at specified times during the experiment. The antibody panel includes glutathione-S-transferase-π (GSTP1)[4,10], heat shock protein 1B (HSP1B)[11], hepatitis A virus cellular receptor 1 homologue precursor (HAVCR1/aka kidney injury molecule-1 (KIM-1))[4], neutrophil gelatinase associated lipocalin (NGAL)[5,6], cysteine rich protein 61 (CYR61)[7], liver fatty acid binding protein (L-FABP)[8], interleukin-6 (IL-6)[4], IL-8[4], IL-18[4], retinol binding protein (RBP)[3], sodium/hydrogen exchanger 3 (NHE3)[4], and netrin-1[9]. Samples were stored at -80°C.

Urine creatinine concentration was determined to equalize for gel loading, and quantitation of western blots was done by densitometry with a Bio-Rad GS800 calibrated densitometer. As a proof of principle, we have already validated three urine biomarkers (GSTP1, HSP1B, and HAVCR1) for use in lambs. As a positive control, we used urine from a lamb with severe renal ischemia secondary to accidental overdose with non-steroidal anti-inflammatory drug (flunixin meglumine)[12,13] The LVAD-implanted lamb 35 day study (Lamb 403), included a pre- operative (baseline negative) sample, and the biomarker findings correlated with gross and histology pathology and were demonstrably more sensitive than serum BUN and creatinine levels (Figures 6 and 7). A manuscript (Cooper et al)[14] has been accepted for publication. Though only speculative with one animal, the increased biomarker levels in the first few post-operative hours may be related to surgery, while the increase near day 2 may be device-related. Additional studies are needed to establish correlations.

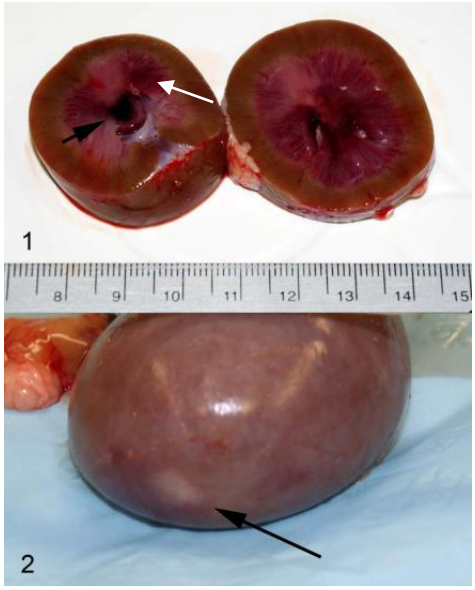

Figure 6. Gross photograph of cross-sectioned kidney from lamb overdosed with flunixin meglumine showing focally extensive hemorrhage in the renal crest (black arrow) with pallor and hemorrhage in the medulla (white arrow). The cortex is grossly normal. Scale is in centimeters.

Gross photograph of the kidney in the LVAD implanted lamb showing a focal area of cortical pallor and depression consistent with chronic infarction (black arrow). Lesion was confirmed by histology.

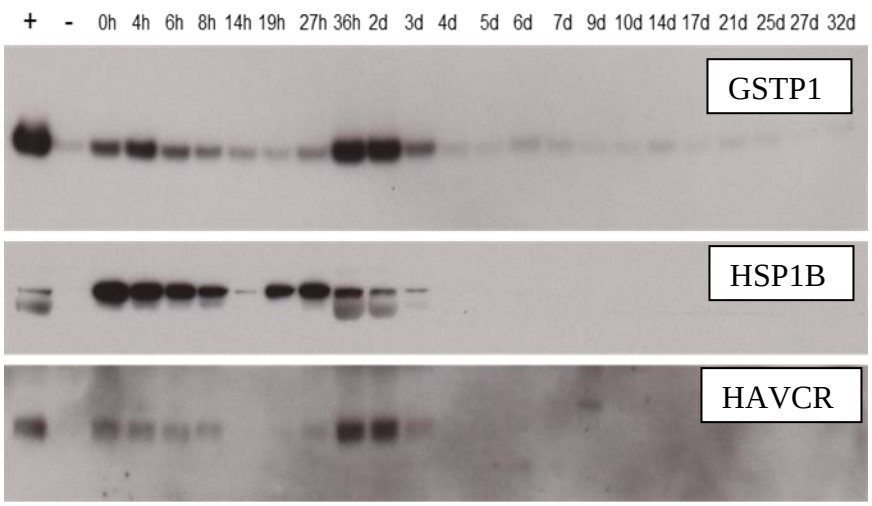

Figure 7. Western blots of urine from NSAID treated nephrotoxicity lamb (+) and from LVAD implanted lamb 24 hours prior to surgery (-) and at denoted times post-operatively. Positive control sample loaded at 0.5 µg creatinine. All LVAD lamb samples loaded at 1.6 µg creatinine. Serum BUN and creatinine values for the LVAD implanted never exceeded normal reference ranges.

Summary. We successfully completed the design of the apical and arterial cannulae for the Infant PVAD. Prototypes were manufactured and tested *in vivo*. Despite the loss of one animal, the results of the successful study demonstrated that the new cannulae are suitable for surgical use, and that thromboembolism is very low, even with low levels of heparin anticoagulation. We do not anticipate any major changes to the cannulae or connector designs at this point. We also measured biomarkers for renal ischemic injury which are promising as more sensitive measures of device embolization.

References

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7. Muramatsu Y, Tsujie M, Kohda Y, et al.: Early detection of cysteine rich protein 61 (CYR61, CCN1) in urine following renal ischemic reperfusion injury. *Kidney Int* 62: 1601-10, 2002.
8. Negishi K, Noiri E, Doi K, et al.: Monitoring of urinary L-type fatty acid-binding protein predicts histological severity of acute kidney injury. *Am J Pathol* 174: 1154-9, 2009.
9. Reeves WB, Kwon O, Ramesh G: Netrin-1 and kidney injury. II. Netrin-1 is an early biomarker of acute kidney injury. *Am J Physiol Renal Physiol* 294: F731-8, 2008.
10. Holmquist P, Torffvit O: Tubular function in diabetic children assessed by Tamm-Horsfall protein and glutathione S-transferase. *Pediatric nephrology (Berlin, Germany)* 23: 1079-83, 2008.
11. Barrera-Chimal J, Perez-Villalva R, Cortes-Gonzalez C, et al.: Hsp72 is an early and sensitive biomarker to detect acute kidney injury. *EMBO molecular medicine* 3: 5-20.
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14. Cooper T, Zhong Q, Nabity M, Rosenberg G, Weiss W: Use of urinary biomarkers of renal ischemia in a lamb preclinical LVAD model. .*Artificial Organs* Accepted for publication, 2012.

18. Extent of Clinical Activities Initiated and Completed. Items 18(A) and 18(B) should be completed for all research projects. If the project was restricted to secondary analysis of clinical data or data analysis of clinical research, then responses to 18(A) and 18(B) should be "No."

18(A) Did you initiate a study that involved the testing of treatment, prevention or diagnostic procedures on human subjects?

_____Yes
___X__No

18(B) Did you complete a study that involved the testing of treatment, prevention or diagnostic procedures on human subjects?

_____Yes
___X__No

If "Yes" to either 18(A) or 18(B), items 18(C) – (F) must also be completed. (Do NOT complete 18(C-F) if 18(A) and 18(B) are both "No.")

18(C) How many hospital and health care professionals were involved in the research project?

_____Number of hospital and health care professionals involved in the research project

18(D) How many subjects were included in the study compared to targeted goals?

_____Number of subjects originally targeted to be included in the study
_____Number of subjects enrolled in the study

Note: Studies that fall dramatically short on recruitment are encouraged to provide the details of their recruitment efforts in Item 17, Progress in Achieving Research Goals, Objectives and Aims. For example, the number of eligible subjects approached, the number that refused to participate and the reasons for refusal. Without this information it is difficult to discern whether eligibility criteria were too restrictive or the study simply did not appeal to subjects.

18(E) How many subjects were enrolled in the study by gender, ethnicity and race?

Gender:
_____Males
_____Females
_____Unknown

Ethnicity:
_____Latinos or Hispanics
_____Not Latinos or Hispanics
_____Unknown

Race:
_____American Indian or Alaska Native
_____Asian
_____Blacks or African American
_____Native Hawaiian or Other Pacific Islander
_____White
_____Other, specify:_____
_____Unknown

18(F) Where was the research study conducted? (List the county where the research study was conducted. If the treatment, prevention and diagnostic tests were offered in more than one county, list all of the counties where the research study was conducted.)

19. Human Embryonic Stem Cell Research. Item 19(A) should be completed for all research projects. If the research project involved human embryonic stem cells, items 19(B) and 19(C) must also be completed.

19(A) Did this project involve, in any capacity, human embryonic stem cells?

_____Yes
__X__ No

19(B) Were these stem cell lines NIH-approved lines that were derived outside of Pennsylvania?

_____Yes

_____ No

19(C) Please describe how this project involved human embryonic stem cells:

20. Articles Submitted to Peer-Reviewed Publications.

20(A) Identify all publications that resulted from the research performed during the funding period and that have been submitted to peer-reviewed publications. Do not list journal abstracts or presentations at professional meetings; abstract and meeting presentations should be listed at the end of item 17. **Include only those publications that acknowledge the Pennsylvania Department of Health as a funding source** (as required in the grant agreement). List the title of the journal article, the authors, the name of the peer-reviewed publication, the month and year when it was submitted, and the status of publication (submitted for publication, accepted for publication or published.). Submit an electronic copy of each publication, listed in the table, in a PDF version 5.0.5 format, 1,200 dpi. Filenames for each publication should include the number of the research project, the last name of the PI, the number of the publication and an abbreviated research project title. For example, if you submit two publications for PI Smith for the "Cognition and MRI in Older Adults" research project (Project 1), and two publications for PI Zhang for the "Lung Cancer" research project (Project 3), the filenames should be:

Project 1 – Smith – Publication 1 – Cognition and MRI
Project 1 – Smith – Publication 2 – Cognition and MRI
Project 3 – Zhang – Publication 1 – Lung Cancer
Project 3 – Zhang – Publication 2 – Lung Cancer

If the publication is not available electronically, provide 5 paper copies of the publication.

Note: The grant agreement requires that recipients acknowledge the Pennsylvania Department of Health funding in all publications. Please ensure that all publications listed acknowledge the Department of Health funding. If a publication does not acknowledge the funding from the Commonwealth, do not list the publication.

Title of Journal Article:	Authors:	Name of Peer-reviewed Publication:	Month and Year Submitted:	Publication Status (check appropriate box below):
1.Use of urinary biomarkers of renal ischemia in a lamb preclinical LVAD model	Cooper T, Zhong Q, Nabity M, Rosenberg G, Weiss W	Artificial Organs	Sep 2011	☐Submitted ☐ Accepted X Published

20(B) Based on this project, are you planning to submit articles to peer-reviewed publications in the future?

Yes____X_____ No_____

If yes, please describe your plans:

The results of studies under this grant would be added to additional future studies and published as a group.

21. Changes in Outcome, Impact and Effectiveness Attributable to the Research Project. Describe the outcome, impact, and effectiveness of the research project by summarizing its impact on the incidence of disease, death from disease, stage of disease at time of diagnosis, or other relevant measures of outcome, impact or effectiveness of the research project. If there were no changes, insert "None"; do not use "Not applicable." Responses must be single-spaced below, and no smaller than 12-point type. DO NOT DELETE THESE INSTRUCTIONS. There is no limit to the length of your response.

None

22. Major Discoveries, New Drugs, and New Approaches for Prevention Diagnosis and Treatment. Describe major discoveries, new drugs, and new approaches for prevention, diagnosis and treatment that are attributable to the completed research project. If there were no major discoveries, drugs or approaches, insert "None"; do not use "Not applicable." Responses must be single-spaced below, and no smaller than 12-point type. DO NOT DELETE THESE INSTRUCTIONS. There is no limit to the length of your response.

None

23. Inventions, Patents and Commercial Development Opportunities.

23(A) Were any inventions, which may be patentable or otherwise protectable under Title 35 of the United States Code, conceived or first actually reduced to practice in the performance of work under this health research grant? Yes_____ No___X_____

If "Yes" to 23(A), complete items a – g below for each invention. (Do NOT complete items a - g if 23(A) is "No.")

a. Title of Invention:
b. Name of Inventor(s):

c. Technical Description of Invention (describe nature, purpose, operation and physical, chemical, biological or electrical characteristics of the invention):

d. Was a patent filed for the invention conceived or first actually reduced to practice in the performance of work under this health research grant?
Yes_____ No____
If yes, indicate date patent was filed:

e. Was a patent issued for the invention conceived or first actually reduced to practice in the performance of work under this health research grant?
Yes_____ No____
If yes, indicate number of patent, title and date issued:
Patent number:
Title of patent:
Date issued:

f. Were any licenses granted for the patent obtained as a result of work performed under this health research grant? Yes_____ No____

If yes, how many licenses were granted?_____

g. Were any commercial development activities taken to develop the invention into a commercial product or service for manufacture or sale? Yes___ No____

If yes, describe the commercial development activities:

23(B) Based on the results of this project, are you planning to file for any licenses or patents, or undertake any commercial development opportunities in the future?

Yes____X_____ No_____

If yes, please describe your plans:

We are pursuing commercial partnerships to further develop the PVAD system.

24. Key Investigator Qualifications. Briefly describe the education, research interests and experience and professional commitments of the Principal Investigator and all other key investigators. You may insert the NIH biosketch form here; please limit to 2 pages.

.BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
William J. Weiss, Ph.D.	Howard E. Morgan Professor of Surgery and Bioengineering
eRA COMMONS USER NAME (credential, e.g., agency login) BWEISS	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
The Pennsylvania State University University Park, PA	BS MS PhD	05/85 12/88 08/95	Electrical Engineering Bioengineering Bioengineering

A. Personal Statement

B. Positions and Honors

Positions and Employment

1979 - 1980 Field Service Engineer, American Scientific Products, Columbia, MD
1980 - 1983 Biomedical Engineer, The Pennsylvania State University, Hershey, PA
1986 - 1989 Senior Biomedical Engineer, The Pennsylvania State University, Hershey, PA
1989 - 1996 Research Assistant, The Pennsylvania State University, Hershey, PA
1996 - 1998 Research Associate, The Pennsylvania State University, Hershey, PA
1998 – 2003 Assistant Professor, College of Engineering, Bioengineering, The Pennsylvania State University, University Park, PA
1998 – 2006 Co-Director, Biomedical Engineering Institute, Pennsylvania State University, Hershey, PA
2001 - 2005 Associate Professor, College of Medicine, Surgery, The Pennsylvania State University, Hershey, PA
2003 – 2006 Associate Professor, College of Engineering, Bioengineering, The Pennsylvania State University, University Park, PA
2005 – 2006 Howard E. Morgan Associate Professor of Surgery, College of Medicine, The Pennsylvania State University, Hershey, PA
2006 - 2008 Director, Biomedical Engineering Institute, The Pennsylvania State University, Hershey, PA
2006 - Present Howard E. Morgan Professor of Surgery, College of Medicine, The Pennsylvania State University, Hershey, PA

Other Experience and Professional Memberships

1987 – Present Institute of Electrical and Electronic Engineers
1992 – Present Sigma Xi, The Scientific Research Society, Pennsylvania State University Chapter
1998 – Present American Society for Artificial Internal Organs
2003 – Present American Institute for Medical and Biological Engineering
2003 – Present American Institute of Ultrasound in Medicine
2005 – Present International Society for Heart and Lung Transplantation

2002 – 2005	Ad hoc member, SBIR/STTR Special Study Section W – Cardiovascular Devices NIH
2003 – Present	Fellow, American Institute for Medical and Biological Engineering
2009 – Present	Board of Trustees, American Society for Artificial Internal Organs
2010 – Present	Executive Committee, American Society for Artificial Internal Organs
2010 – 2011	Deputy Program Chair, American Society for Artificial Internal Organs
2011 – 2012	Program Chair, American Society for Artificial Internal Organs
2011 - 2012	Chair, SBIR Study Section, Special Emphasis Panel

C. Selected peer-reviewed publications (in chronological order).

1. Weiss WJ, Rosenberg G, Snyder AJ, Cleary TJ, Gaumond RP, Geselowitz DB, Pierce WS. Permanent circulatory support systems at the Pennsylvania State University. *IEEE Trans Biomed Eng*. 1990;37(2):138-145.

2. Pierce WS, Snyder AJ, Rosenberg G, Weiss WJ, Pae WE, Waldhausen JA. A long-term ventricular assist system. *J Thorac Cardiovasc Surg*. 1993;105(3):520-524.

3. Snyder AJ, Rosenberg G, Weiss WJ, Ford SK, Nazarian RA, Hicks DL, Marlotte JA, Kawaguchi O, Prophet GA, Sapirstein JS, et al. In vivo testing of a completely implanted total artificial heart system. *ASAIO J*. Jul-Sep 1993;39(3):M177-184.

4. Weiss WJ, Rosenberg G, Snyder AJ, Donachy J, Sr, Reibson J, Kawaguchi O, Sapirstein JS, Pae WE, Pierce WS. A completely implanted left ventricular assist device. Chronic in vivo testing. *ASAIO J*. 1993;39(3):M427-432.

5. Weiss WJ, Rosenberg G, Snyder AJ, Rawhouser M, Pierce WS, Kusagawa H, Mehta S, Prophet GA, Marlotte JA, Nazarian RA, Ford SK, Hicks DL. Recent improvements in a completely implanted total artificial heart. *ASAIO J*. 1996;42(5):M342-346.

6. Rosenberg G, Snyder AJ, Weiss WJ, Kusagawa H, Rawhouser MA, Prophet GA, Mehta S, Reibson JD, Cleary TJ. Dynamic in vitro and in vivo performance of a permanent total artificial heart. *Artif Organs*. 1998;22(1):87-94.

7. Weiss WJ, Rosenberg G, Snyder AJ, Pierce WS, Pae WE, Kuroda H, Rawhouser MA, Felder G, Reibson JD, Cleary TJ, Ford SK, Marlotte JA, Nazarian RA, Hicks DL. Steady state hemodynamic and energetic characterization of the Penn State/3M Health Care Total Artificial Heart. *ASAIO J*. 1999;45(3):189-193.

8. Mehta SM, Weiss WJ, Snyder AJ, Prophet GA, Pae WE, Jr., Rosenberg G, Pierce WS. Testing of a 50 cc stroke volume completely implantable artificial heart: expanding chronic mechanical circulatory support to women, adolescents, and small stature men. *ASAIO J*. 2000;46(6):779-782.

9. Mehta SM, Pae WE, Jr, Rosenberg G, Snyder AJ, Weiss WJ, Lewis JP, Frank DJ, Thompson JJ, Pierce WS. The LionHeart LVD-2000: a completely implanted left ventricular assist device for chronic circulatory support. *Ann Thorac Surg*. 2001;71(3 Suppl):S156-161; discussion S183-154.

10. Snyder A, Pae WE, Boehmer J, Rosenberg G, Weiss W, Pierce W, Thompson J, Lewis J, Frank D, Zintak H, Scholl S, Korfer R, El-Banayosy A, Arusoglu L, Fey O, Morshuis M. First clinical trials of a totally implantable destination therapy ventricular assist system. *J Congest Heart Fail Circulatory Supp*. 2001;1:185-192.

11. Izraelev V, Weiss WJ, Fritz B, Newswanger RK, Paterson EG, Snyder A, Medvitz RB, Cysyk J, Pae WE, Hicks D, Lukic B, Rosenberg G, Izraelev V, Weiss WJ, Fritz B, Newswanger RK, Paterson EG, Snyder A, Medvitz RB, Cysyk J, Pae WE, Hicks D, Lukic

B, Rosenberg G. A passively suspended Tesla pump left ventricular assist device. *ASAIO J*. Nov-Dec 2009;55(6):556-561. PMCID: PMC2789418

12. Baldwin JT, Borovetz HS, Duncan BW, Gartner MJ, Jarvik RK, Weiss WJ. The national heart, lung, and blood institute pediatric circulatory support program: a summary of the 5-year experience. Circulation 2011;123:1233-40.

13. Weiss WJ, Carney EL, Clark JB, Peterson R, Cooper TK, Nifong TP, Siedlecki CA, Hicks D, Doxtater B, Lukic B, Yeager E, Reibson J, Cysyk J, Rosenberg G, Pierce WS. Chronic In Vivo Testing of the Penn State Infant Ventricular Assist Device. *ASAIO Journal.* Jan-Feb. 2012;58:65-72

14. Cooper TK, Zhong Q, Nabity M, Rosenberg G, Weiss WJ. Use of urinary biomarkers of renal ischemia in a lamb preclinical left ventricular assist device model. *Artif Organs*. 2012 Sep;36(9):820-824.

15. Cooper TK, Griffith JW, Reibson J, Peterson R, Roush EP, Zhong Q, Weiss WJ, Rosenberg G. Antibiotic-associated eosinophilic and occlusive arteritis in calves complicating preclinical studies of left ventricular assist devices. *Toxicol Path*. 2012 June 14. [Epub ahead of print]

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Christopher A. Siedlecki	Professor of Surgery and Bioengineering
eRA COMMONS USER NAME (credential, e.g., agency login) csiedlecki	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
Milwaukee School of Engineering, Milwaukee, WI	B.S.	05/91	Biomedical Engineering
Case Western Reserve Univ., Cleveland, OH	M.S.	05/94	Biomedical Engineering
Case Western Reserve Univ., Cleveland, OH	Ph.D.	08/96	Biomedical Engineering

A. Personal Statement

B. Positions and Honors

Positions and Employment

1991 – 1996	Graduate Research Assistant, Dept of Biomedical Engineering, Case Western Reserve Univ
1996 – 1997	Postdoctoral Research Associate, Dept Biomedical Engineering, Case Western Reserve Un.
1997 – 1999	Postdoctoral Scientist, Eli Lilly and Company Research Labs, Indianapolis, IN
1998 – 1999	Industrial Fellow, Center for Interfacial Engineering, Department of Chemical Engineering and Materials Science, University of Minnesota
1999 – 2005	Assistant Professor of Surgery and Bioengineering, The Pennsylvania State University,
2005 - 2010	Associate Professor of Surgery and Bioengineering with tenure, The Pennsylvania State University
2010 – present	Professor of Surgery and Bioengineering with tenure, The Pennsylvania State University

Other Experience and Professional Memberships

Associate Editor, Journal of Biomedical Materials Research B, Applied Biomaterials
Editorial Board, Journal of Biomedical Materials Research A, Colloids and Surfaces B: Biointerfaces
Ad-Hoc Reviewer, Molecular, Cellular and Developmental Neuroscience 3 (MDCN-3) Study Section, 2000, Hematology Small Business (ZRG1 HEME-D) Study Section, 2005-07. Special Emphasis Panel-Technology Development for Biomedical Applications Award 2005-10, Hemostasis and Thrombosis (HT) Study Section 2008-2010, Biomaterials and Biointerfaces Study Section 2009, NSF Panel Reviewer 2009
Program Committee, Annual Meeting of the Society for Biomaterials, 1997, 2001, 2005. 2007; 2010; ASAIO Meeting 2005; Program Chairperson, Bioengineering Track, ASAIO Meeting, 2009

Honors

1991 – 1994	National Institutes of Health, Graduate Research Training Grant
1994	Society for Biomaterials Student Research Award, Undergraduate, Masters or Clinical Health Trainee Category, 20th Annual Meeting of the Society for Biomaterials
2009	Special Interest Group Representative to the Board of Directors, Society for Biomaterials

C. Selected Peer-reviewed Publications (Selected from ~50 peer-reviewed publications)

Most relevant to the current application

1. Milner KR, Snyder AJ, Siedlecki CA. Sub-micron texturing for reducing platelet adhesion to polyurethane biomaterials. *J Biomed Mater Res A.* 2006;76(3):561-570.
2. Xu LC, Siedlecki CA. Atomic force microscopy studies of the initial interactions between fibrinogen and surfaces. *Langmuir*. 2009;25(6):3675-3681. PMCID: PMC2749234
3. Agnihotri A, Soman P, Siedlecki CA. AFM measurements of interactions between the platelet integrin receptor GPIIbIIIa and fibrinogen. *Colloids Surf B Biointerfaces*. 2009;71(1):138-147. Epub 2009 Feb 3.
4. Xu LC, Siedlecki CA. Microphase restructuring of hydrated polyurethane biomaterials: phase restructuring, protein activity and platelet adhesion. *Acta Biomater*. 2010;6(6):1938-1947. Epub 2009 Dec 3.
5. Xu LC, Siedlecki CA. Microphase separation structure influences protein interactions with poly(urethane urea) surfaces. *J Biomed Mater Res A.* 2010;92(1):126-136.

Additional recent publications of importance to the field (in chronological order)

1. Agnihotri A, Siedlecki CA. Time-dependent conformational changes in fibrinogen measured by atomic force microscopy. *Langmuir.* 2004;20(20):8846-8852.
2. Agnihotri A, Siedlecki CA. Adhesion mode atomic force microscopy study of dual component protein films. *Ultramicroscopy*. 2005;102(4):257-268.
3. Miller R, Guo Z, Vogler EA, Siedlecki CA. Plasma coagulation response to surfaces with nanoscale chemical heterogeneity. *Biomaterials*. 2006;27(2):208-215.
4. Agnihotri A, Garrett JT, Runt J, Siedlecki CA. Atomic force microscopy visualization of poly(urethane urea) microphase rearangments under aqueous conditions. *J Biomater Sci Polym Ed.* 2006;17(1-2):227-238.
   Xu LC, Soman P, Runt J, Siedlecki CA. Characterization of surface microphase structures of poly(urethane urea) biomaterials by nanoscale indentation with AFM. *J Biomater Sci Polym Ed.* 2007;18(4):353-368.
   Xu LC, Siedlecki CA. Effect of surface wettability and contact time on protein adhesion to biomaterial surfaces. *Biomaterials*. 2007;28(22):3273-3283. Epub 2007 Apr 12.
5. Soman P, Rice Z, Siedlecki CA. Measuring the time-dependent functional activity of adsorbed fibrinogen by atomic force microscopy. *Langmuir*. 2008;24(16):8801-8806. Epub 2008 Jul
6. Chatterjee K, Guo Z, Vogler EA, Siedlecki CA. Contributions of contact activation pathways of coagulation factor XII in plasma. *J Biomed Mater Res A.* 2009;90(1):27-34.
7. Vogler EA, Siedlecki CA. Contact activation of blood plasma coagulation-leading opinion paper. *Biomaterials*. 2009;30(10):1857-1869. Epub 2009 Jan 24. PMCID: PMC2705825
8. Chatterjee K, Thornton J, Vogler EA, Siedlecki CA. Moderation of prekallikrein-factor XII interactions in surface activation of coagulation by protein-adsorption competition. *Biomaterials*. 2009;30(28):4915-4920. Epub 2009 Jun 23. PMCID: PMC2749226

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Gerson Rosenberg, Ph.D.	C. McCollister Evarts, MD Professor in Artificial Organs Professor of Surgery and Bioengineering Chief, Division of Artificial Organs
eRA COMMONS USER NAME (credential, e.g., agency login) GERSON	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
The Pennsylvania State University, University Park, PA	Associate	05/66	Drafting & Design
The Pennsylvania State University, University Park, PA	B.S.	06/70	Mechanical Engineering
The Pennsylvania State University, University Park, PA	M.S.	03/72	Mechanical Engineering
The Pennsylvania State University, University Park, PA	Ph.D.	11/75	Mechanical Engineering

A. Personal Statement

B. Positions and Honors

1970-1972	Graduate Assistant, Mechanical Engineering, The Pennsylvania State University, University Park, PA
1972-1973	Instructor, Mechanical Engineering, The Pennsylvania State University, University Park, PA
1973-1975	Research Assistant, Mechanical Engineering, The Pennsylvania State University, University Park, PA
1975-1976	Post Doctoral Scholar, Mechanical Engineering, The Pennsylvania State University, University Park, PA
1976-1978	Senior Project Associate, College of Medicine, The Pennsylvania State University, Hershey, PA
1978-1983	Research Associate, College of Medicine, The Pennsylvania State University, Hershey, PA
1981-Present	Associate Member, Faculty Graduate School, The Pennsylvania State University, University Park, PA
1981-1983	Assistant Professor of Bioengineering, College of Medicine, The Pennsylvania State University, Hershey, PA
1983-1988	Senior Research Associate, College of Medicine, The Pennsylvania State University, Hershey, PA
1983-1988	Associate Professor of Bioengineering, College of Medicine, The Pennsylvania State University, Hershey, PA
1983-1991	Assistant Chief, Division of Artificial Organs, College of Medicine, The Pennsylvania State University, Hershey, PA
1988-Present	Professor, College of Medicine, The Pennsylvania State University, Hershey, PA

1988-Present	Professor of Bioengineering, College of Engineering, The Pennsylvania State University, University Park, PA
1991-Present	Chief, Division of Artificial Organs, Department of Surgery, College of Medicine, The Pennsylvania State University, Hershey, PA
1997-2006	Jane A. Fetter Professor of Surgery, College of Medicine, The Pennsylvania State University, Hershey, PA
1998-2006	Director, Biomedical Engineering Institute, College of Medicine, The Pennsylvania State University, Hershey, PA
2006-Present	C. McCollister Evarts, M.D. Professor in Artificial Organs, College of Medicine, The Pennsylvania State University, Hershey, PA
2006-2008	Co-Director, Biomedical Engineering Institute, College of Medicine, The Pennsylvania State University, Hershey, PA
1982-Present	Member, Sigma Xi – The Scientific Research Society of North America Outstanding Alumnus 1982, Ogontz Campus, The Pennsylvania State University
1992	Founding Fellow, American Institute of Medical and Biological Engineering
2002	"Engineer of the Year", *Design News Magazine*
2003	Alumni Fellow, Penn State Alumni Association, Penn State Abington
2004-2005	President, American Society for Artificial Internal Organs
2005-Present	Investment Director, American Society for Artificial Internal Organs

C. <u>Selected peer-reviewed Publications</u>

1. Undar A, Rosenberg G, Myers JL. Part 1: principles of research on pulsatile and non-pulsatile perfusion during chronic support. *ASAIO J.* May-Jun 2005;51(3):303-304; author reply 305-308.
2. Yamanaka H, Rosenberg G, Weiss W, Snyder A, Zapanta CM, Siedlecki C. Short-term *in vivo* studies of surface thrombosis in a left ventricular assist system. *ASAIO J.* May-Jun 2006;52(3):257-265.
3. Deutsch S, Tarbell JM, Manning KB, Rosenberg G, Fontaine AA. Experimental fluid mechanics of pulsatile artificial blood pumps. *Annu Rev Fluid Mech*. Jan 2006;38:65-86.
4. Izraelev V, Weiss WJ, Fritz B, Newswanger RK, Paterson EG, Snyder A, Medvitz RB, Cysyk J, Pae WE, Hicks D, Lukic B, Rosenberg G. A passively-suspended Tesla pump left ventricular assist device. *ASAIO J*. Nov-Dec 2009;55(6):556-561. PMCID: PMC2789418
5. Fritz B, Cysyk J, Newswanger R, Weiss W, Rosenberg G. Development of an inlet pressure sensor for control in a left ventricular assist device. *ASAIO J*. May-Jun 2010;56(3):180-185. PMCID: PMC2873045

<u>Most relevant to the current application</u>

1. Yamanaka H, Rosenberg G, Weiss WJ, Snyder AJ, Zapanta CM, Siedlecki CA. Multiscale analysis of surface thrombosis in vivo in a left ventricular assist system. *ASAIO J.* Sep-Oct 2005;51(5):567-577.
2. Zapanta CM, Griffith JW, Hess GD, Doxtater BJ, Khalapyan T, Pae WE, Rosenberg G. Micro-textured materials for circulatory support devices: preliminary studies. *ASAIO J.* Jan-Feb 2006;52(1):17-23.
3. Undar A, Ji, B, Lukic B, Zapanta CM, Kunselman AR, Reibson JD, Weiss WJ, Rosenberg G, Myers JL. Quantification of perfusion modes in terms of surplus hemodynamic energy levels in a simulated pediatric CPB model. *ASAIO J*. Nov-Dec 2006;52(6):712-717.

4. Undar A, Ji B, Lukic B, Zapanta CM, Kunselman AR, Reibson JD, Khalapyan T, Baer L, Weiss WJ, Rosenberg G, Myers JL. Comparison of hollow-fiber membrane oxygenators with different perfusion modes during normothermic and hypothermic CPB in a simulated neonatal model. *Perfusion.* 2006;21:(6):381-390.
5. Rosenberg G. Tissue engineering and artificial organs. Chapter 63: Cardiac valve prostheses. Chapter 64: Artificial heart and circulatory assist devices. In: Bronzino JD, ed. *The Biomedical Engineering Handbook.* 3rd ed. Boco Raton, FL: CRC Press; 2006.
6. Connell JM, Khalapyan T, Al-Mondhiry H, Wilson RP, Rosenberg G, Weiss WJ. Anticoagulation of juvenile sheep and goats with heparin, warfarin, and clopidogrel. *ASAIO J*. Mar-Apr 2007;53(2):229-237.
7. Connell JM, Pae WE, Rosenberg G. Comparison of LionHeart LVAD-implanted calves based on renal infarctions. *ASAIO J.* Mar-Apr 2007;53(2):147-151.
8. Lukic B, Zapanta CM, Khalapyan T, Connell J, Pae WE, Myers JL, Wilson RP, Undar A, Rosenberg G, Weiss WJ. The effect of left ventricular function and drive pressures on the filling and ejection of a pulsatile pediatric ventricular assist device in an acute animal model. *ASAIO J.* May-Jun 2007;53(3):379-384.
9. Connell JM, Khalapyan T, Myers JL, Rosenberg G, Weiss WJ. Anatomic fit assessment for the Penn State pediatric ventricular assist device. *ASAIO J*. Nov-Dec 2007;53(6):687-691.
10. Haut-Donahue TL, Dehlin W, Gillespie J, Weiss WJ, Rosenberg G. Finite element analysis of stresses developed in the blood sac of a left ventricular assist device. *Med Eng Phys*. May 2009;31(4):454-460. PMCID: PMC2702508