Application for the Hasso Plattner Design Thinking Research GRANT Program for the project:

Surgical Treatment of Congestive Heart Failure: Design of a Novel Intracardial Ventricular Assist Device

Project Team:

- Wolfgang Bothe, MD, Postdoctoral Research Fellow, Department of Cardiothoracic Surgery, Stanford University School of Medicine. wbothe@stanford.edu
- D. Craig Miller, MD, Doelger Professor of Cardiovascular Surgery, Department of Cardiothoracic Surgery, Stanford University School of Medicine, Director of the Cardiovascular Surgical Physiology Research Laboratory. dcm@stanford.edu
- Ellen Kuhl, PhD, Assistant Professor in the Departments of Mechanical Engineering and Bioengineering at Stanford University. ekuhl@stanford.edu
- Paul G. Yock, MD, Martha Meier Weiland Professor of Medicine, Department of Bioengineering, Stanford University. yock@stanford.edu
- James Wall, MD, Biodesign Innovation Fellow in the Department of Bioengineering, Stanford University, jkwall@stanford.edu
- Rebecca E. Taylor, MSc, PhD student in Mechanical Engineering, Stanford University. rebeccat@stanford.edu
- Mohan Kotikanyadanam Varadaraju, BSc, Master/PhD student in Mechanical Engineering, Stanford University. varadarajumk@gmail.com
Abstract

Ventricular assist devices (VADs) are a surgical treatment option for patients with end-stage congestive heart failure. At present, however, all VADs suffer from considerable shortcomings: the devices are expensive, technically complex, require extensive surgery and postoperative care and are prone to serious complications like stroke or severe infections. VADs are therefore only eligible for a small number of patients and significantly impair quality of life. Our vision is to develop a new VAD that is cost-effective, safe, durable and easily implantable and, thus, offers an attractive treatment option for patients suffering from heart failure worldwide. Motivated by the ideas of rapid conceptual prototyping, we recently designed a prototype that follows an entirely new concept. This device generates cardiac output via a cable shortening mechanism that exerts tensile force on the myocardium from the inside of the left ventricle (LV). Stemming from the radically innovative nature of this concept, multiple questions pose a great challenge in terms of design thinking:
How can it be achieved that the myocardium withstands the applied tensile forces? What is the optimal material for the inserted cables? How should the shortening of the cables be generated? Where should the cables insert?

These questions will be addressed in close collaborative multidisciplinary experiments – in vitro, in silico, and in vivo. Application outcomes of different designs of the prototype and its individual components will be quantitatively measured using histological cross sections and standard hemodynamic monitoring. Through a successful design thinking process at the intersection of design, medicine/biology, and engineering we aim to jointly provide a unique treatment option for people suffering from one of the largest global health problems of the 21st century – congestive heart failure.

Proposal narrative

Introduction

Congestive heart failure affects about 5 million people in the United States and is the leading cause of death in industrial countries[1]. The definitive therapy for the end stage of heart failure remains cardiac transplantation; however, this option is only available for a small population of patients. The increasing prevalence of heart failure and the declining availability of donor organs have driven the development of ventricular assist devices (VADs) that are capable of supporting the heart mechanically [1-3]. Since the first VAD implantation in 1966 by Michael deBakey [4] a plethora of different devices has been introduced and tested in animal as well as in human studies [5]. VADs are available either as extra- or intracorporeal devices (Figure 1). All VADs that are currently implanted are expensive, technically complex and require extensive surgery and postoperative care. Extracorporeal VADs (Figure 1A) are particularly prone to infections [6] and significantly impair the quality of life. Intracorporeal VADs are either available as continuous (Figure 1C) or pulsatile (Figure 1B) flow generating devices [7]. Continuous flow generating VADs need substantial anticoagulation and the associated risks (such as bleeding or stroke) are considerable [6, 8]. There are only few intracorporeal devices on the market that generate physiologic pulsatile blood flow (e.g. Thoratec Heartmate, Figure 1B). These devices are rather large and must therefore be implanted into the abdomen. The implantation sites are prone to infections and the device has significant
mechanical reliability issues [9]. Furthermore, due to its size, these devices are not applicable for smaller patients and can only be implanted in the left (but not the right) ventricle. VADs are therefore only eligible for a limited number of patients and significantly impair the quality of life. Despite those apparent shortcomings that are mainly due to inherent suboptimal designs, those VADs represent the preliminary end-result of a long design process. As the current market leaders mainly focus on further refining their existing products, the design process of VADs has slowed down significantly in the recent years.

Objective
Our objective is to design a VAD that is cost-effective, safe, durable, and easily implantable in any patient suffering from end-stage congestive heart failure worldwide. In pursuit of this objective, we aim to develop a VAD that is based on the unique design concept to be fully intracardially implantable and using the heart as a sheath to generate cardiac output. Such a VAD would not only closely mimic physiologic mechanisms of myocardial output generation, but also require minimal implantation of foreign material and therefore significantly reduce the risk of bleeding or thrombus formation.

Preliminary results
Motivated by the ideas of rapid conceptual prototyping, we designed a first prototype and demonstrated that a VAD based on this concept is in principle feasible to generate cardiac output. The components of this prototype as well as the mechanisms to generate cardiac output and the advantages over conventional VADs are described in the following.

Figure 2: Schematic of the prototype and its three main components: I) Mechanical mitral valve with four aluminum tubes that are attached to the valve frame. II) Four cables that are conducted via the tubes through the left ventricle (LV) and connected to III) anchors that are punched through the LV wall. The prototype is connected to the LV by sewing the mechanical valve to the mitral annulus. A bag is sewn to the left atrium and filled with water. Ao indicates Aorta, MV mitral valve.

Components of the prototype used
Figure 2 shows a schematic of the developed prototype and its three main components: I) A mechanical mitral valve with four aluminum tubes attached to the valve frame; II) Four cables that are conducted via tubes through the LV in a diagonally crossing fashion to generate ventricular torsion; III) Anchors that were built to distribute shear forces acting on the myocardium are punched through the LV wall. The cables are attached to the intraventricular site of these anchors. The prototype is connected to the LV by sewing the mechanical valve to the mitral annulus. A bag is sewn to the left atrium and filled with water.

Mechanism to generate cardiac output
Figure 3 shows a schematic of the mechanism of forward output generation: Manual application of cable tension induces un-twisting of the diagonal cables as the anchors move up and inward. Inspired by force generation in the healthy heart, cardiac output is generated by a combined shortening,
compression, and torsion mechanism. Figure 4 shows the successful output generation in a freshly excised, non-beating ovine heart using our recently developed prototype.

**Advantages over conventional VADs**
- The device is fully implantable.
- The hybrid tension-torsion mechanism that generates pump function closely mimics the physiological myocardial output generation.
- The implantation of foreign material is minimal.
- The device is implantable in both ventricles and in any patient (children and adults).
- The device is designed for permanent use.
- Percutaneous implantation may be possible in the future.

**Conclusion**
We aim, for the first time, to design a VAD that is intracardially implantable and that uses the heart as a sheath to generate pulsatile cardiac output. Due to this new and innovative concept this device offers multiple advantages over conventional VADs. Furthermore, it generates numerous new and challenging questions in terms of design thinking: How can it be achieved that the myocardium withstands the applied tensile forces, i.e. what is the best design for the anchors? What is the optimal material for the cables inserted? How should the pulling mechanism of the cables ideally be generated? Where should the cables be inserted and how many should be used? These questions require different points of view and will subsequently be addressed in a strong, multidisciplinary cooperation *in vitro, in silico*, and *in vivo*. This way we aim to achieve our vision to not only build a device that has the potential to enter the huge, but almost untapped market of VADs built for destination therapy, but, more importantly, offers a unique treatment option for patients worldwide suffering from end stage heart failure.

**Team**
Our unique team of experts works at the intersection of design, medicine/biology, and engineering to jointly solve one of the biggest 21st century problems of global health: the treatment of congestive heart failure. Different design aspects within this project will be addressed by our interdisciplinary working group. The entire team will jointly be introduced to patients suffering from end-stage heart failure and observe clinical open heart surgeries that include the implantation of current VADs. This will serve as basis for our design thinking process. In regular brainstorm meetings each member will be updated about the progress of our project.

- Wolfgang Bothe, MD, Postdoctoral Research Fellow in the Department of Cardiothoracic Surgery, current teamleader and responsible surgeon (large animal experiments) in Dr. Millers research laboratory. Role: Principal investigator
• D. Craig Miller, MD, Doelger Professor of Cardiovascular Surgery in the Stanford University School of Medicine and the Director of the Cardiovascular Surgical Physiology Research Laboratory. He is a world-renowned expert in cardiothoracic surgery and cardiovascular research. Role: advisor
• Ellen Kuhl, PhD, Assistant Professor in the Departments of Mechanical Engineering and Bioengineering at Stanford University. She has world-renowned expertise in finite element analysis related to biomechanics. Role: Co-investigator
• James Wall, MD, Biodesign Innovation Fellow in the Department of Bioengineering, Stanford University, Founder and Chief Executive Officer of a medical device company. He has completed most of his training as a general surgeon and is taking a two-year break from clinical duties to pursue his interest in medical device development through the Stanford Biodesign and Innovation program. Role: Co-investigator
• Paul G. Yock, MD, Martha Meier Weiland Professor of Medicine, Department of Bioengineering, Stanford University. He is a world-renowned authority in the field of biodesign and cardiovascular research. Role: advisor
• Rebecca E. Taylor, MSc, PhD student in Mechanical Engineering, Stanford University
• Mohan Kotikanyadanam Varadaraju, BSc, Master/PhD student in Mechanical Engineering, Stanford University

Research Plan
The project is divided into five stages (milestones) building upon our initial idea and first prototype.

Figure 5 shows a sketch of the timeline with milestones and end-year deliverables of our planned project. Please see Appendix 1 for further detail.
Appendix
Appendix 1: Timeline with milestones and year-end deliverable

- **Milestone 1:** To refine the three basic mechanical components of Prototype 1 as described below and to connect the refined prototype to a Langendorff Perfusion Apparatus.
  - **Component I:** We will build a device that can generate cable shortening automatically over a period of hours/days. Force, velocity and rate of cable shortening will be adjustable. The implantation methodology of this component will be optimized. A unique mechanism will be designed where the mechanical valve can be anchored to the native valve with a stick mechanism. This will not only reduce mechanical forces acting on the mitral annulus (where the valve is usually surgically sewn on), but also make the procedure easier and safer.
  - **Component II:** The material of the cables used will be optimized. A finite element simulation provides a unique virtual test environment to explore different cable materials in silico before testing them in vivo using freshly excised, non-beating hearts and our prototype.
  - **Component III:** The anchors will be made smaller as well as safer and easier to implant. Different designs (Figure 6) will be tested with our prototype. The local effects of the anchors on the myocardium will be assessed in histological cross sections.

  The connection of the prototype to a Langendorff Perfusion Apparatus will allow to keep the myocardium viable (and, thus, determine the feasibility of the methodology used) over a time period of hours up to days. The generated pressure and cardiac output will be assessed with commercially available pressure transducers and by measuring the ejected volume, respectively. Tests will be performed on the isolated, non-beating heart (end-year deliverable, year 1: Prototype 2).

- **Milestone 2:** To equip the force generating unit with a feedback mechanism (EKG trigger) that allows cable shortening along with the regular myocardial contraction. VAD contraction must start early after the phase of isovolumetric contraction. This phase takes no longer than ~70ms (at a heart rate between 90-110bpm) which needs to be considered for the feedback design. This series of experiments will be performed on the isolated, beating heart using our Langendorff Apparatus (end-year deliverable, year 2: Prototype 3).

- **Milestone 3:** To reduce the size of force generating unit. As this unit will initially be built in a rather simple manner to allow repetitive in vitro testing it needs to be completely redesigned. A potential mechanism to generate cable shortening is explained and illustrated in Figure 7. The VAD will be built in the Stanford Prototype realization Laboratory. The research facilities of Professor Craig Millers laboratory provide a unique environment to implant and test the VAD in a large animal model (end-year deliverable, year 3: VAD 1).

- **Milestones 4 and 5** are long-term goals and not part of the 3y funding period.
Appendix 2: Budget

This budget was constructed and estimated for a 3-year funding period. A cost-of-living increase of 3% was assumed for salaries, according to guidelines approved by Stanford University. All effort and expenses charged to this project will be for services specific to the research. Facilities and major equipment are available for the performance of the sponsored agreement at no direct cost to the sponsor. As the design of the implantable VAD (Year 3) is expected to be highly sophisticated and expensive components with state-of-the-art technology will be needed, the budget in year 3 slightly exceeds the grant limits.

A. Salaries

The budget requests salary for the PI Wolfgang Bothe and two weeks of summer salary support for Ellen Kuhl for one month over the period of three years. Ellen is responsible for the tests in silico. Support is requested for Mohan Kotikanyadanam Varadaraju, Mechanical Engineering Master/PhD student. He will be intimately involved into all procedures of the project, including in silico testing, prototype building and all in vitro and in vivo test series. Professor Torsten Doenst will help in the first year as visiting expert to integrate our prototype into a Langendorff Perfusion model.

B. Supplies

A total of 1500$/year is requested for printing, publications, posters. Furthermore, money is requested for creativity workshops that will be organized in regular intervals.

C. Equipment

Financial support for equipment is requested for all technical components that are needed for the prototype building, i.e. for anchors, cables, force generating unit, Langendorff Perfusion histological cross sections etc..

D. Travel

An annual travel cost of $7000 is budgeted for the PI, Master/Phd (Mohan) and Phd (Rebecca) student travel. Travel cost covers student participation at the Annual Meeting of the American Heart Association, the American Association of Thoracic Surgery and the European Association of Cardiothoracic Surgery where Mohan and Rebecca will participate in student poster and podium presentation competitions to disseminate our work.

| A: | Year 1/2/3 |
|---|---|---|
| Principal Investigator (Wolfgang Bothe, MD) | $60,000/61,800/63,800 | |
| Master/Phd student (Mohan Varadaraju) | $35,000/36,000/37,500 | |
| Visting Professor (Torsten Doenst, MD) | $5,000 | |
| Assistant Professor (Professor Ellen Kuhl, PhD) | $6,000/6,180/6,400 | |
| B: | Printing, publications, posters | $1,500/1,500/1,500 |
| Creativity workshop | $5,000/5,000/5,000 |
| C: | Access Prototype Realization Laboratory | $300/300/300 |
| Anchors, cables, force generating unit | $8,000/8,000/- |
| Feedback mechanism for force generating unit | $/-/15,000/15,000 |
| Langendorff Perfusion | $10,000/-/- |
| Histological cross sections | $5000/5000/5000 |
| Pressure transducers | $4000/-/- |
| Components of implantable VAD | $/-/-/20,000 |
| D: | National: | $5,000/5000/5000 |
| International: | $7000/7000/7000 |
| Total: | $151,800/150,800/166,500 |
Appendix 3: References


Wolfgang Bothe, MD

EDUCATION

2001-2006: Assistentzarzt (Surgical Resident) in the Department of Cardiovascular Surgery, University Hospital Freiburg, Germany

2004 – 9/2006: Director of the section “Arrhythmia-surgery” in the Department of Cardiovascular Surgery, University Hospital Freiburg, Germany

2001: Doctorate Degree (Dr.med. “magna cum laude”). Dissertation: High-Dose Insulin Therapy for Patients Undergoing Heart Surgery

9/2006 – present: Postdoctoral Research Fellow, Department of Cardiothoracic Surgery, Stanford School of Medicine, Stanford, Teamleader and responsible surgeon of the experimental ovine study: Effects of newly designed mitral annuroplasty rings on left ventricular and mitral valvular geometry and dynamics

ORIGINAL CONTRIBUTIONS


Bothe W, Schlensak C, Doenst T, Beyersdorf F. A Fistula Between the Circumflex Artery and the Coronary Sinus Mimics Coronary Artery Disease in a 60y-old Patient, Interactive Cardiovascular and Thoracic Surgery, 2005; 4: 81–82


Bothe W, Krishnamurthy G, Chang PA, Swanson JC, Davis LR, Itoh A, Ingels NB, Miller DC. Effects of the GeoForm Annuloplasty Ring on Anterior Mitral Leaflet Stresses and Strains in the Normal Ovine Heart. submitted


PRESENTATIONS

Bothe W, Beyersdorf F, Doenst T. High-Dose Glucose-Insulin-Potassium for Patients Undergoing Heart Surgery: Effects on Glucose and Potassium Homeostasis, „22nd European Section Meeting of the International Society for Heart Research“, Szeged, Ungarn, 2002

Bothe W, Doenst T, Beyersdorf F. High-Dose Insulin Therapy After Cardiac Surgery for Patients with Impaired Left Ventricular Function, „International Symposium on Myocardial Protection from Ischemia-Reperfusion Injury“, Ashville, USA, 2.-6.6. 2002


GRANTS

9/2006 – present: funded by research grant S06/07 from the “Deutsche Herzstiftung”, Frankfurt, Germany

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D. Craig Miller, Thelma and Henry Doelger Professor of Cardiovascular Surgery

Stanford University Medical School, Stanford, CA B.A. 1969 Medical Sciences
Stanford University Medical School, Stanford, CA M.D. 1972 Medicine

A. Positions and Honors.

Positions and Employment
1972-1977 General, Cardiac, Thoracic, and Vascular Surgery Residency, Stanford
1978-1983 Assistant Professor of Cardiovascular Surgery, Stanford University
1983-1988 Associate Professor of Cardiovascular Surgery, Stanford University
1989-1998 Professor of Cardiovascular Surgery, Stanford University
1998-present Doelger Professor of Cardiovascular Surgery, Stanford University

Other Experience and Professional Memberships
1992-1996 NIH SAT Study Section Charter Member
1988-1991 VA Merit Review Board, Surgery Research Study Section
1990-1991 Chairman, VA Surgery Merit Review Board
1984-1991 Editorial Advisory Board: J Thorac and Cardiovascular Surgery
1990-1993 Editorial Board: Circulation
1990-1992 Chairman, AHA Cardiovascular Surgery Program Committee
1992-1993 Co-Chairman, AHA Committee on Scientific Sessions
1990-1992 Guest Editor, Circulation: Cardiovascular Surgery Supplement
1995-1997 Chairman, AHA Cardiovascular Surgery Council
1994-1995 President, Western Thoracic Surgical Association
1998-2005 Associate Editor, J Thoracic and Cardiovascular Surgery

American Board of Surgery (1978); American Board of Thoracic Surgery (1979); Special Qualifications in General Vascular Surgery (1983, American Board of Surgery)

Honors and Awards
Stanford University Medical School Distinguished Alumni Award, 1997
Wilfred Bigelow Award, Canadian Cardiovascular Society, 2000
Antoine Marfan Award, National Marfan’s Foundation, 2001
William W. L. Glenn Lecturer, American Heart Association (Cardiovascular Surgery Council), 2002
Distinguished Scientist of the American Heart Association 2003
- 664 peer-reviewed publications

B. Research Support
5 RO1 HL-29589-23 9/15/03 – 07/31/08
NIH/NHLBI
VENTRICULAR DYNAMICS FROM SURGICALLY INSERTED MARKERS
Role: PI
The primary goals of this multi-year project were further elucidation of LV systolic and diastolic mechanics in man and animals after various cardiac operations, definition and assessment of LV systolic torsional deformation and diastolic recoil, characterization of the importance of the mitral subvalvular apparatus in terms of LV systolic pump function, and the mechanisms causing acute ischemic MR (IMR) in animal models.

1 RO1 HL67025-04 6/01/01 – 03/31/11
NIH/NHLBI
Chronic Ischemic MR – Mechanisms and Novel Surgical Therapy
Role: PI
The goal of this related project is to determine the geometric valvular (annular, leaflet, and subvalvular LV) mechanisms responsible for chronic ischemic mitral regurgitation (CIMR) and to differentiate and define the therapeutic effects of ring annuloplasty versus a trans-annular suture reparative technique (SLAC).
Ellen Kuhl, Phd

Assistant Professor
Department of Mechanical Engineering

Professional Preparation
TU Kaiserslautern, Germany  Mechanical Engineering  Dr.-Ing. habil.  2004
University of Stuttgart, Germany  Civil Engineering  Dr.-Ing.  2000
University of Hannover, Germany  Civil Engineering  Dipl.-Ing.  1995

Appointments
09/07-  Affiliate Faculty, Bioengineering, Stanford University, Stanford, CA.
01/07-  Assistant Professor, Mechanical Engineering, Stanford University, Stanford, CA.
11/02-10/05 Assistant Professor (Level I), Mechanical Engineering, TU Kaiserslautern, Germany
02/04-04/04 Visiting Researcher, Aerospace Engineering, Caltech, CA.
01/01-04/01 Habilitation Researcher, Mechanical Engineering, TU Kaiserslautern, Germany
04/00-03/01 Researcher, Aerospace Engineering, TU Delft, The Netherlands
02/05-04/05 Visiting Researcher, Aerospace Engineering, Caltech, CA.
11/05-12/06 Assistant Professor (Level II), Mechanical Engineering, TU Kaiserslautern, Germany
01/07-  Assistant Professor, Civil Engineering, University of Stuttgart, Germany
01/07-  PhD Researcher, Civil Engineering, University of Hannover, Germany

Professional Societies
American Society of Mechanical Engineers (ASME)
European Society of Biomechanics (ESB)
German Association for Applied Mathematics and Mechanics (GAMM)

Selected Publications and Presentations

Synergistic Activities
- **Collaborators:** Stanford: Christopher Zarins, Joseph Wu, Neil Ingels, Craig Miller, Christopher Jacobs, Marc Levenston, Beth Pruitt
- **Graduate and Postdoctoral Advisors:** Ekkehard Ramm, PhD advisor, Rene de Borst, Postdoc mentor at TU Delft, Paul Steinmann, Habilitation mentor at TU Kaiserslautern.

Public and Professional Service
- **Guest editor:** "Computer simulations of mechanobiology" in Computer Methods in Biomechanics and Biomedical Engineering and “Mechanics in biology: Cells and tissues” in Philosophical Transactions of the Royal Society
- **Reviewer:** National Science Foundation, ENG/CMMI and BIO/MCB, since 2007
- **Reviewer:** German Science Foundation DFG, since 2005
- **Session organization:** “Biomechanics”, GAMM Annual Meeting, Berlin, 2006
- **Minisymposia organization:** MS009 “Growth and remodeling” and MS106 “Multiscale modeling of materials” in the honor of Kaspar J. Willam’s 65th birthday, USNCCM IX, San Francisco, 2007
- **Miniworkshop organization:** “The mathematics of growth and remodeling of soft biological tissues”, Oberwolfach, Germany, 2008
- **Scientific committee:** “IUTAM Symposium on cellular, molecular and tissue mechanics”, 2008
- **Stanford ME Graduate Admission Committee, since 2007
- **Stanford ME ABET Committee, since 2007
- **Society of Women Engineers:** SWE Fellowship Committee, SWE Undergraduate Lunches, SWE Elementary school outreach program “Exploring New Worlds”, since 2007

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Paul G. Yock, Martha Meier Weiland Professor of Medicine (Cardiovascular)

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**BIOGRAPHICAL SKETCH**

<table>
<thead>
<tr>
<th>NAME</th>
<th>POSITION TITLE</th>
</tr>
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<tbody>
<tr>
<td>Paul G. Yock, MD</td>
<td>Martha Meier Weiland Professor of Medicine (Cardiovascular)</td>
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**EDUCATION/TRAINING**

<table>
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<tr>
<th>INSTITUTION AND LOCATION</th>
<th>DEGREE</th>
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<tr>
<td>Amherst College, MA</td>
<td>A.B.</td>
<td>1969-73</td>
<td>Philosophy/Chemistry</td>
</tr>
<tr>
<td>Harvard Medical School, Boston, MA</td>
<td>M.D.</td>
<td>1975-79</td>
<td>Medicine</td>
</tr>
<tr>
<td>University of California at San Francisco</td>
<td>Intern Res.</td>
<td>1979-80</td>
<td>Medicine</td>
</tr>
<tr>
<td>Stanford University Medical Center, CA</td>
<td>Fellow</td>
<td>1982-85</td>
<td>Cardiology</td>
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</tbody>
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A. Positions and Honors

**Positions and Employment**

- 1986-1994: Assistant and Associate Professor of Medicine (Cardiology), University of California, San Francisco
- 1994-1998: Associate Professor of Medicine (Cardiovascular), Stanford University School of Medicine
- 1998-present: Professor of Medicine (Cardiovascular)
- 1996-present: Professor of Mechanical Engineering (By Courtesy)
- 2002-present: Leadership Council, Bio-X Program, Director, Biosensor Unit
- 2003-present: Co-Chair, Department of Bioengineering

**Honors and Awards (recent, selected)**

- 2000: Martha Meier Weiland Professor of Medicine, Stanford University
- 41 Patents

**Other Experience and Professional Memberships (selected)**

- Fellow, American College of Cardiology
- Fellow, American Institute for Medical and Biological Engineering
- Editorial Advisory Boards, Circulation, Journal of the American College of Cardiology, American Heart Journal

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G. Research Support

**Sponsor, Research Award**

- No Identifying Number (Yock Co-PI)
  - Yamanouchi, Inc.
  - Determining the efficacy of intramyocardial delivery for treatment of cardiomyopathy
  - Role: Co-PI
  - 01/00-02 - 12/01

- 120-99 (Yock PI)
  - The American Foundation
  - Biomedical Device Development Program
  - Role: PI

- No Identifying Number (Yock PI)
  - American Heart Association
  - Intramyocardial Delivery of the Coronary Microcirculation
  - Role: Co-PI
  - 01/01-02 - 12/01

- S25-057-Ha (Yock PI)
  - National Science Foundation
  - SM@D, Bioengineering: Innovation, Design and Entrepreneurship Alliance Annual Meeting
  - Role: PI
  - 02/01-03 - 02/03

- No Identifying Number (Yock PI)
  - Edwards Life Sciences
  - Novel Therapies for the Treatment of Cardiomyopathy
  - Role: PI
  - 03/01-06 - 02/08

- No Identifying Number (Yock PI)
  - KIK Pharmaceuticals, Inc.
  - Localized Intramyocardial Delivery of Anti-Reperfusion Injury
  - Role: PI
  - 03/15/06 - 03/14/06

- No Identifying Number (Yock PI)
  - Fox Hollow Technology
  - Evaluation of Novel Interventional Cardiac Devices
  - Role: PI
  - 01/01-01 - 01/02

- D226211 (Yock PI)
  - Kaiser Foundation
  - Development and Improvement of Medical Device
  - Role: PI
  - 09/01-05 - 10/01

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James Wall, MD

Education

2006 - 2008
Stanford University
Biodesign Innovation Fellowship
MSE Bioengineering

2003 – 2008-present
University of California San Francisco
Internship and Residency in General Surgery

1999 - 2003
University of Pennsylvania
MD

1995 - 1999
Tulane University
BSE Biomedical Engineering
  • Summa Cum Laude • Honors Conferred

Research Experience

2003
Univ. College Cork Dept. of Surgery Cork, Ireland
Clinical Sepsis Research
  • Designed randomized, double blinded, clinical trial of the anti-endotoxin agent taurolidine in patients undergoing major trans-abdominal surgery.
  • Recruited early series of patients and performed trial including flow cytometry analysis of inflammatory cytokines and clinical outcome measurements.

May - Sept. 2000
Institute for Medicine and Engineering
Biomedical Research Fellowship
  • Designed and implemented swine model of atherosclerosis
  • Incorporated model into study of differential gene expression between normal vasculature and atherosclerotic plaques

June - Sept. 1998
Duke University Durham, NC
Cardiacelectrophysiology Research Group
  • Developed complex mathematical model of cardiac tissue based on electric circuit theory for examination of arrhythmias
  • Postulated improvements in defibrillation therapy

Business experience

2006 - present
InSite Medical Technologies
  • Founder and Chief Executive Officer
  • Co-inventor and developer of a novel device for accessing the epidural space
  • Award $100K National Science Foundation Small Business Innovation Research Award
  • Raised $1M in Seed financing from combined angel and venture investors

Mar. 2007 - present
Kleiner, Perkins, Caufield, & Byers
  • Intern
  • Developed concepts and business strategies to address needs surrounding the pandemic influenza and bio defense fund and assisted a Series B investment in Breathe Technologies.
  • Board Member (Observer) Breathe Technologies
  • Performed diligence on diverse life science investments

2001 - 2003
docTOUR
  • Founder
  • Formulated and co-wrote business plan for the physician affinity marketing group, docTOUR
  • Received semi-finalist recognition in the Wharton Business Plan Competition
  • Developed business as part of the Wharton Venture Initiation Program and brought on senior management team

Awards received

Class of 1971 memorial academic scholarship – merit based medical school scholarship
President Agnew Surgical Society - University of Pennsylvania
NCAA Division I athletic conference academic medal of honor (tennis)
Tau Beta Pi National Engineering Honor Society

Grants

National Science Foundation Small Business Innovation Research Grant
Principal Investigator for a $100K Phase I SBIR award entitled ‘Improving the safety and efficacy of epidural anesthesia’
National Collegiate Inventors and Innovators Alliance Advanced E-Team Grant
$18,500 technology development grant for a device to accurately access the epidural space for administration of anesthesia

Patents

A device to access the epidural space US filing 10220-703 based on US provisional patent 60/872,317: 2007
A device for controlled minimally invasive access US provisional patent filed
A device for tissue approximation US provisional patent filed