

BIOGRAPHICAL SKETCH

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NAME: Arash Kheradvar, M.D., Ph.D., FAHA

eRA COMMONS USER NAME (credential, e.g., agency login): ARASH00

POSITION TITLE: Professor of Biomedical Engineering and Medicine, University of California, Irvine

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

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Tehran University of Medical Sciences, Tehran, Iran	M.D.	08/2000	Medicine
California Institute of Technology, Pasadena, CA, USA	Ph.D.	11/2006	Bioengineering
California Institute of Technology, Pasadena, CA, USA	Postdoctoral	10/2007	Cardiovascular Engineering

A. Personal Statement

I am a physician-scientist and currently a tenured professor at UC Irvine. I have devoted my career to cardiovascular science and engineering. My major research background and interests are on development of novel cardiac imaging technologies, heart valve engineering, and cardiac biomechanics. I have been the lead inventor and co-inventor of multiple imaging technologies related to this proposed project, such as Echo-PIV, 4D Flow MR and artificial intelligence applications in cardiac imaging.

My other major contributions to the field of cardiovascular are: (1) Echocardiographic Particle Image Velocimetry (Echo-PIV); (2) cardiac biofluid mechanics that resulted in characterization of cardiovascular vortex formation and vortex imaging, which are internationally recognized by the cardiovascular community; (3) development of novel heart valve technologies, including a fully-repositionable/retrievable transcatheter aortic valve (FOLDAVALVE), a stent-less transcatheter mitral valve (aVALVE), a surgical bi-leaflet dynamic mitral valve (DYNAMITRAL) and more recently, an IVUS-guided TAVR technology. These technologies are either licensed to startup companies or very close to translation to industry.

I have published over 48 peer-reviewed journal articles and am the lead inventor of more than 45 issued, pending and provisional patents, mostly on heart valves, transcatheter delivery systems and cardiac imaging modalities.

- Kheradvar A.** On the accuracy of intracardiac flow velocimetry methods, *Journal of Echocardiography*, 2017 June;15(2): 67-69. PMID: 28205061
- Falahatpisheh A and **Kheradvar A.** A Framework for Synthetic Validation of 3D Echocardiographic Particle Image Velocimetry. *Meccanica*, 2017 Feb, 52(3): 555–561.
- Kheradvar A**, Houle H, Pedrizzetti G, Tonti G, Belcik T, Ashraf M, Lindner JR, Gharib M, Sahn DJ. Echocardiographic Particle Image Velocimetry: A Novel Technique for Quantification of Left Ventricular Blood Vorticity Pattern, *J of American Society of Echocardiography* 2010, 23(1) 86-94. PMID: 19836203
- Kheradvar A**, Groves EM, Falahatpisheh A, Mofrad MRK, Alavi SH, Tranquillo R, Dasi LP, Simmons, CA, Goergen, CJ, Baaijens, F, Little SH, Canic S, Griffith B. Emerging Trends in Heart Valve Engineering: Part IV. Computational Modeling and Experimental Studies, *Annals of Biomedical Engineering*, 2015 Oct;43(10):2314-2333. PMID: 26224522
- Falahatpisheh A, Pedrizzetti G, **Kheradvar A.** Three-Dimensional Reconstruction of Cardiac Flows Based on Multi-Planar Velocity Fields, *Experiments in Fluids*, November 2014, 55:1848.

B. Positions and Honors

Positions and Employment

- 1993-00 Medical Student, Tehran University of Medical Science, Tehran, IRAN
- 2000-02 Research Fellow, Immunogenetics Laboratory, Dept. of Immunology, Tehran University of Medical Sciences, Tehran, IRAN
- 2002-06 Graduate Research Assistant, Cardiovascular and Biofluid Dynamics Laboratory, Caltech, Pasadena, CA
- 2006-07 Postdoctoral Scholar, Cardiovascular and Biofluid Dynamics Laboratory, Caltech, Pasadena, CA
- 2007-10 Assistant Professor of Mechanical Engineering, Internal Medicine and Cell Biology & Anatomy, University of South Carolina, Columbia, SC
- 2010-13 Assistant Professor of Biomedical Engineering and Medicine, University of California, Irvine
- 2011-13 Assistant Professor of Mechanical and Aerospace Engineering, University of California, Irvine
- 2011-13 Honorary Research Associate, California Institute of Technology, Pasadena, CA, USA
- 2012-15 Honorary Research Fellow of Cardiac MR, Royal Brompton Hospital, London, UK
- 2013-17 Associate Professor (tenured) of Biomedical Engineering and Medicine, UC Irvine
- 2017- Professor of Biomedical Engineering and Medicine, UC Irvine

Other Experience and Professional Memberships

Editorial Duties:

- 2005-13 Editorial Board Member, ASAIO Journal
- 2017- Associate Editor, Annals of Biomedical Engineering

Study Sections:

- 2006 National Medical Research Council of Ministry of Health, Singapore;
- 2007- National Science Foundation (NSF)
- 2009-10 NIH Study Section Member ZRG1 SBIB-V (58) Challenge Grants Panel 23
- 2009-15 NIH Study Section Member ZRG1 VH-D (50, 55) NHBLI System Biology.
- 2009- American Heart Association's Radiology, Imaging and Surgery Committee
- 2016- NICHD 3D Printing Study Section (ZHD1 DSR-K(51))
- 2017- Science Foundation Ireland

Founder and co-founder:

- 2009- ENGcore, LLC
- 2009- Folda, LLC
- 2010-13 WALVE, Corp

Professional Membership:

- 2006- Member, American Society for Artificial Internal Organs
- 2009- Member, American Heart Association
- 2011- Member, Society of Heart Valve Disease
- 2011- Member, European Mechanics Society
- 2014- Member, American Society of Echocardiography
- 2015- Member, American Physiological Society
- 2016 Fellow, Humboldt Foundation

Consultant and Advisory Boards:

- 2004- Edwards Lifesciences Corp.
- 2008-13 Ultrawave Labs, Inc.
- 2014- CalHealth, Inc.

Honors

- 2002-06 Benjamin M Rosen graduate fellowship in Bioengineering/Engineering Science at Caltech
- 2009 Vivien Thomas Young Investigator Award Finalist nominated by American Heart Association
- 2012 Transatlantic Career Development Award in Cardiovascular Research from Leducq Foundation
- 2012 Endorsed by *Royal Academy of Engineering* as an "exceptional promise" to be a world leader in Medical Devices and Medical Imaging areas of research.
- 2012-14 Honorary research fellow, Royal Brompton Hospital, London, UK

- 2013- Fellow, American Heart Association; elected by two Councils on *Cardiovascular Radiology and Intervention* and *Cardiovascular Surgery and Anesthesia* of the American Heart Association.
- 2014-16 Research Committee Member of the American Heart Association, Western States Affiliate.
- 2014- Member, UCI's Dean of Engineering's executive committee
- 2016 Fellow, Alexander Humboldt Foundation (experienced researcher fellowship)

C. Contribution to Science

1. One major area of my research is heart valve engineering. I have developed three different heart valves through my career: (1) FOLDAVALVE is a novel 14-French fully retrievable/repositionable valve that prevents the leaflets from being crimped within the stent in a collapsed state by folding them externally to the stent; (2) Hybrid Tissue-Engineering Heart Valve is a patient-specific hybrid heart valve with self-regenerating capacity and a potential for lifelong durability; and (3) DYNAMITRAL is a fully retrievable bio-inspired transcatheter mitral valve with dynamic annulus for transapical implantation. These devices are at different stages of development.
 - a. Alavi SH, Ruiz V, Krasieva T, Botvinick EL, and **Kheradvar A**. Characterizing the Collagen Fiber Orientation in Pericardial Leaflets under Mechanical Loading Conditions, *Annals of Biomedical Engineering*, 2013,41 (3) 547-561. PMID: PMC3963497
 - b. **Kheradvar A**, Groves EM and Tseng E. Proof of Concept of FOLDAVALVE: A Novel 14Fr Totally Repositionable and Retrievable Transcatheter Aortic Valve. *EuroIntervention*, 2015 Mar 16;10(11) pii: 20141002-01. PMID: 25772904
 - c. **Kheradvar A**, Falahatpisheh, A. The Effects of Dynamic Saddle Annulus and Leaflet Length on Transmitral Flow Pattern and Leaflet Stress of a Bi-leaflet Bioprosthetic Mitral Valve, *Journal of Heart Valve Disease*, 2012, 21; 225-233. PMID: 22645859
 - d. Groves EM, Falahatpisheh A, Su JL, **Kheradvar A**. The Effects of Positioning of Transcatheter Aortic Valve on Fluid Dynamics of the Aortic Root, *ASAIO J*. 2014 Sep-Oct;60(5):545-52 (Featured on the cover of the Sep-Oct 2014 issue). PMID: PMC4334568
 - e. Falahatpisheh A, Morisawa D, Toosky TT, **Kheradvar A**. A Calcified Polymeric Valve for Valve-in-Valve Applications, *Journal of Biomechanics*, 2017 Jan; 50(1): 77–82. PMID: 27887725

2. The other major area of focus in my lab is cardiac MRI. We have been working on different aspects of cardiac MRI, including 4D Flow MRI and application of artificial intelligence in segmentation of cardiac MRI. I also was recently awarded a Humboldt fellowship for experienced researchers to study the state of energy in single-ventricle anomalies pre- and post-Fontan procedure. We have been the first group to show that a simplified Bernoulli's equation cannot be used for accurate estimation of transvalvular pressure drop.
 - a. Falahatpisheh A, Rickers C, Gabbert DD, Heng EL, Stalder A, Kramer HH, Kilner PJ, **Kheradvar A**. Simplified Bernoulli's method significantly underestimates pulmonary transvalvular pressure Drop. *Journal of Magnetic Resonance Imaging*, 2016;43:1313–19. (Featured on June 2016 cover) PMID: 26584006
 - b. Hajiaghayi M, Groves EM, Jafarkhani H, and **Kheradvar A**. A 3D Active Contour Method for Automated Segmentation of the Left Ventricle from Magnetic Resonance Images, *IEEE Transactions on Biomedical Engineering*, 2017 Jan; 64 (1): 134-144. PMID: 27046887
 - c. Sievers HH, Putman LM, **Kheradvar A**, et al. 4D flow streamline characteristics of the great arteries twenty years after Lecompte and direct spiral arterial switch operation (DSASO) in simple TGA, *Global Cardiology Science and Practice* 2016 (3):29. (Featured on the cover of the December 2016 issue).
 - d. Rickers C, **Kheradvar A**, Sievers HH, et al. Is the Lecompte Technique the last word on transposition of the great arteries repair for all patients? A magnetic resonance imaging study including a spiral technique two decades postoperatively, *Interactive Cardiovascular and Thoracic Surgery*, 2016 Jun;22(6):817-25. PMID: PMC4986772
 - e. Sievers HH, **Kheradvar A**, Kramer HH and Rickers C. 3D Heart Model and 4D Flow MRI 20 Years after Spiral Arterial Switch Operation. *Thorac Cardiovasc Surg Reports*, 2016 Dec; 05(01): 44-46. PMID: PMC5177426

3. In addition to the contributions described above, my publications are considered the first that quantitatively characterized the presence of the transmitral vortex ring formation during diastole. In 2006, we published the first paper introducing vortex formation time index for diagnosis of diastolic heart failure in PNAS. This paper has been cited over 216 times to date. The concept of "vortex formation time index" is currently translated to cardiology clinics and being used by cardiologists to diagnose diastolic dysfunctions. I have also been a

major player in developing echocardiographic Particle Image Velocimetry to map the flow fields inside the heart chambers, and vortex imaging is my second major achievement.

- a. **Kheradvar A**, Assadi R, Falahatpisheh, A, Sengupta, PP. Assessment of Transmitral Vortex Formation in Patients with Diastolic Dysfunction, *Journal of American Society of Echocardiography*, 2012, 25 (2) 220-7. (Featured on the cover of the February 2012 issue). PMID: 22099070
 - b. **Kheradvar A**, Gharib M. Influence of ventricular pressure-drop on mitral annulus dynamics through the process of vortex ring formation, *Annals of Biomedical Engineering* 2007, 35 (12):2050-2064. PMID: 17899379
 - c. Gharib M, Rambod E, **Kheradvar A**, et al. Optimal vortex formation as an index of cardiac health. *Proceedings of National Academy of Sciences (PNAS)* 2006, 103 (16): 6305-6308. PMID: PMC1458873
 - d. Falahatpisheh A, Pahlevan NM, **Kheradvar A**. Effect of the Mitral Valve's Anterior Leaflet of on Axisymmetry of Transmitral Vortex Ring, *Annals of Biomedical Engineering*, 2015 Oct;43(10):2349-2360. PMID: 25821111
 - e. **Kheradvar A**, Gharib M. On Mitral Valve Dynamics and its connection to Early Diastolic Flow, *Annals of Biomedical Engineering*, 2009 Jan, 37(1):1-13. PMID: 18982451
4. I have also been significantly involved in several aspects of cardiac and heart valve biomechanics. For example, my group has been the first to characterize the heart valves' collagen fiber orientation and their dynamics in response to load using second harmonic generation microscopy. We have also been the first to quantify crimp-induced damage in transcatheter heart valves.
- a. **Kheradvar A**, Groves EM, Falahatpisheh A, Mofrad MRK, Alavi SH, Tranquillo R, Dasi LP, Simmons, CA, et al. Emerging Trends in Heart Valve Engineering: Part IV. Computational Modeling and Experimental Studies, *Annals of Biomedical Engineering*, 2015 Oct;43(10):2314-2333. PMID: 26224522
 - b. Mangual JO, Föll D, Jung B, Pedrizzetti G, **Kheradvar A**. Aging does not Affect Radial Viscoelastic Behavior of the Left Ventricle, *Cardiology*, 2013;125(1):38-49. PMID: 23635990
 - c. Alavi SH, Groves EM, **Kheradvar A**. The Effects of Transcatheter Valve Crimping on Pericardial Leaflets, *The Annals of Thoracic Surgery*, 2014 Apr;97(4):1260-6. PMID: 24444873
 - d. Alavi SH, Soriano Baliarda M, Bonessio N, Valdevit L, **Kheradvar A**. A Tri-leaflet Nitinol Mesh Scaffold for Engineering Heart Valves, *Annals of Biomedical Engineering*, 2017 Feb;45(2):413-426. PMID: 28008545
 - e. **Kheradvar A**, Kasalko J, Johnson D, Gharib M. An in-vitro study of changing profile heights in mitral bioprostheses and their influence on flow. *ASAIO Journal* 2006 Jan-Feb 52(1):34-38 PMID: 16436888
5. I have been significantly involved in design and development of medical devices, in particular, heart valves, cardiac assist devices, and imaging tools for cardiovascular flow visualization. Here is the list of four selected patents from more than 45 issued, published applications and provisional:
- a. **Kheradvar A**. Implantable prosthetic valves and methods; Patent# 8,876,897
 - b. Alavi SH and **Kheradvar A**. Mesh enclosed tissue constructs; Patent# 8,900,862
 - c. **Kheradvar A**, Sutton MA, Membrane-deformation mapping technique, Patent# 8,767,049
 - d. **Kheradvar A**, Gharib M. Monolithic in situ forming valve system; Patent# 7,780,724
 - e. **Kheradvar A**, Sutton MA, Membrane-deformation mapping technique, U.S. Patent# 8,767,049

Partial List of my Published Work:

<http://www.ncbi.nlm.nih.gov/pubmed/?term=kheradvar+a>

<https://scholar.google.com/citations?user=7MVET8kAAAAJ&hl=en>

<http://kheradvar.eng.uci.edu/publications.php>

D. Research Support

Ongoing:

(1) 16GRNT30980070 Kheradvar (PI) 07/01/2016 to 06/30/ 2018

American Heart Association Grant-in-Aid

“Assessing the Risk of Transcatheter Heart Valve Calcification and Biomechanical Failure” (Role: PI)

(2) NIH-1R21EB021513-01A1 Kheradvar (PI) 09/2016 to 08/2018

“Ultrasound-Guided Delivery System for Accurate Positioning/Repositioning of Transcatheter Aortic Valves” (Role: PI)

- (3) 1U54HL119893 Palazzolo (Center PI) 7/1/15 to 12/31/17
NIH Center for Accelerated Innovations: Technology Development Program
“Development of a Self-Regenerative Hybrid Heart Valve” (Role: Project PI)
- (4) 1U54HL119893 Palazzolo (Center PI) 7/1/15 to 12/31/17
NIH Center for Accelerated Innovations: Technology Development Program
“A bio-inspired transcatheter mitral valve” (Role: Project PI)
- (5) 16IRG27250078 Kheradvar (PI) 01/2016 to 12/2017
IVUS-Guided Delivery System for Accurate Positioning/Repositioning of Transcatheter Aortic Valves” (Role: PI)
- (6) Gift Kheradvar (PI) [2014 to present]
Edwards Lifesciences Foundation
“Self-regenerative heart valve technology” (Role: PI)
- (7) 1 T32 HL116270-01A1 Hughes CW (PI) 07/2013 to 6/2018
National Institute of Health: Training Program in Cardiovascular Applied Research and Entrepreneurship
(Role: Co-Investigator and mentor)
- Completed:**
- (1) 14GRNT18800013 Kheradvar (PI) 01/2014 to 01/2016
American Heart Association Grant-in-Aid
“Assessment of the right ventricular flow in patients with RV dysfunction” (Role: PI)
- (2) 16POST27540025 S Hamed Alavi (Fellow) 01/2016 to 03/2017
American Heart Association postdoctoral grant
“Tissue Engineered Heart Valve with a Non-Degradable Scaffold” (Role: Mentor)
- (3) N/A Kheradvar (PI) 01/2014 to 06/2016
Children’s Heart Foundation grant
“A Self-Regenerative Hybrid Heart Valve” (Role: PI)
- (4) N/A Kheradvar (PI) 08/2011 to 02/2016
Wallace H Coulter Foundation: Coulter Translational Research Award
“Development of a Novel Self-expandable Bioprosthetic Heart Valve for Percutaneous Delivery and Implantation”
(Role: PI)
- (5) 14POST20530013 Ahmad Falahatpisheh (Fellow) 07/2014-06/2016
American Heart Association postdoctoral grant
“Computation of kinetic energy dissipation inside the right heart of patients with repaired tetralogy of Fallot”
(Role: Mentor)
- (6) 13PRE14630049 Ahmad Falahatpisheh (Fellow) 01/2012-12/2013
American Heart Association predoctoral grant
“Modeling the flow inside the right heart of patients with repaired tetralogy of Fallot” (Role: Mentor)
- (7) 10BGIA4170011 Kheradvar (PI) 07/2010 to 07/2012
American Heart Association BGIA
“Development of 3D Echocardiographic Particle Image Velocimetry (Echo-PIV) for Assessment of Right Ventricular Flow Pattern” (Role: PI)
- (8) N/A (Kheradvar, PI) 07/2012 to 01/2015
Leducq Foundation Transatlantic Career Award
“Flow through the right heart after repair of tetralogy of Fallot: An Image-based modeling approach” (Role: PI)