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 (cardiology)

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 Professor of Biomedical Engineering and Medicine at the University of California, Irvine. My research focuses on cardiovascular science and engineering and capitalizes on my multidisciplinary background in bioengineering and medicine. My current research interests are on developing novel cardiac imaging technologies for post-processing cardiac MRI and echocardiography, as well as engineering new generation of heart valves that are safer, more durable and can address the current unmet clinical needs. My lab has developed several platforms for post-processing cardiac MRI and echocardiography, particularly for analysis of congenital heart disease.

While an Assistant Professor, I received a Leducq Foundation's career development grant to study the flow through the right heart of patients with repaired Tetralogy of Fallot using the software developed in my lab for processing 4D Flow MRI. That study was performed at the Royal Brompton Hospital in London, UK in collaboration with Dr. Philip Kilner. Later on, while an Associate Professor, I received an experienced researcher award from Germany's Alexander von Humboldt Foundation to study the fluid dynamics of hypoplastic left heart syndrome in collaboration with Prof. Dr. Carsten Rickers. More recently, as a Professor, I was awarded a Fulbright Distinguished Chair in Health Sciences to work with colleagues at the University of Eastern Finland.

At its base, my research aims to address fundamental questions on biomechanical cues related to effects of blood flow on heart disease and cardiac malformation. My major contribution to the field on that ground is characterization of cardiovascular vortex formation and its effects in adults and children, and vortex imaging though echocardiographic Particle Image Velocimetry (Echo-PIV), and heart valve engineering. More recently, we focused on the reciprocal effects between scaffold geometry and ventricular vortex flow on viability and performance of a tissue-engineered mitral valve, which is supported by NHLBI (1R01HL162687-01A1). Additionally, our research efforts have focused on deciphering the synergistic interaction between hemodynamics and genetics that form the heart and accordingly how congenital cardiac malformations occur. An NSF grant (2109959) has been awarded to us to study early changes in gene expression in response to altered blood flow, and early changes in blood flow in response to altered signaling that may lead to congenital heart disease.

Further, I am the sole PI of an NHLBI grant (1R01HL153724-01A1) to study the state of energy in the right ventricle of patients with pulmonary arterial hypertension using Echo-PIV. My other active imaging projects are related to a cloud-based AI platform for automatic segmentation and analysis of pediatric Cardiac MRI datasets, funded by the American Heart Association (19AIML35180067) and Clinical Evaluation of Echocardiography system Aplio i900 funded by Canon Medical Systems USA, Inc.

The translational aspect of my research involves heart valve engineering, developing novel biomedical technologies for cardiac imaging, and cardiac support devices. I am the lead inventor of several structural heart devices, including a fully repositionable and retrievable transcatheter aortic valve (*FoldaValve*), a modular transcatheter valve system for atrioventricular valves (*AValve*), a hybrid tissue-engineered heart valve (*H-TEHV*), and an active cardiac support device (*HelixCardia*). More recently, we have been developing a growth-accommodating transcatheter pulmonary valve for very young children with congenital heart disease (*IRIS Valve*) funded by NICHD (1R21HD105889-01). I was also awarded an NHLBI mPI R01 grant (1R01HL157631-01A1) along with Prof. Boyce Griffith (PI) and Prof. Aaron Fogelson (mPI) to computationally and experimentally model subclinical leaflet thrombosis in bioprosthetic aortic valves.

Over my career, I have published over **70** peer-reviewed journal articles; am the lead inventor of **38** issued U.S. patents, mostly on cardiac imaging and heart valve systems; and have authored **2** books: (1) *Vortex Formation in the Cardiovascular System* (ISBN: 9781447122883), published by Springer Cardiology; and (2) *Principles of Heart Valve Engineering* (ISBN: 9780128146613), published by Elsevier. My H-index is 37 and i10-index is 71.

- Arafati A, Morisawa D, Avendi MR, Amini, MR, Assadi RA, Jafarkhani H, **Kheradvar A**. Generalizable Fully Automated Multi-Label Segmentation of 4-Chamber View Echocardiograms based on Deep Convolutional Adversarial Networks. *Journal of the Royal Society Interface*, 2020, Aug; 17 (169): 20200267. PMID: 32811299
- Karimi-Bidhendi A., Arafati A., Cheng A., Wu Y., **Kheradvar A.***, Jafarkhani H.* Fully-Automated Deep-Learning Segmentation of Pediatric Cardiac MRI of Patients with Complex Congenital Heart Diseases. *Journal of Cardiovascular Magnetic Resonance*, 2020, in press. (*co-corresponding author)
- Avendi MR, **Kheradvar A**, Jafarkhani H. A Combined Deep-Learning and Deformable-Model Approach to Fully Automatic Segmentation of the Left Ventricle in Cardiac MRI, *Medical Image Analysis*, 2016 Feb 6;30:108-119. PMID: 26917105
- Arafati A, Hu P, Finn JP, Rickers C, Cheng AL, Jafarkhani H, **Kheradvar A**. Artificial Intelligence in Pediatric and Adult Congenital Cardiac MRI: An Unmet Clinical Need, *Cardiovascular Diagnosis and Therapy*, 2019, *Cardiovascular Diagnosis and Therapy*, 2019 October Vol 9, Supplement 2. PMID: 31737539

B. Positions and Honors

Positions and Employment

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

Other Experience and Professional Memberships

Editorial Board Memberships:

2017- Associate Editor, Annals of Biomedical Engineering
2022- Editorial Board Member, Journal of Cardiovascular Development
2004- Journal Reviewer (70+ journals): Science, PNAS, JCMR, JACC, JACC Basic to Translational Science, Proceedings of the Royal Society of London A, Lancet, JAHA, Scientific Reports, Circulation, Circulation Cardiovascular Imaging, Circulation Cardiovascular Intervention, Experimental Mechanics, JCTR, International Journal of Cardiovascular Imaging, Journal of Mechanics in Medicine

and Biology, Journal of Fluid Mechanics, JMRI, Journal of Royal Society Interface, IEEE Transactions on Biomedical Engineering, IEEE Transactions of Medical Imaging, European Heart Journal Cardiovascular Imaging, Acta BioMaterialia, etc. 2005-13 ASAIO Journal

Study Sections:

2022- NIH Study Section Member 10 ZHL1 CSR-O (O2) 1, Catalyze: Product Definition
2021- NIH Study Section Member ZRG1 SBIB-D (02) M Member Conflict: Bioengineering, Surgery, Anesthesiology and Trauma
2021- NIH Study Section Member ZTR1 DPI-3 (01) UH2/UH3 applications for Intramural - Extramural Collaboration for Drug Screening with Biofabricated 3-D Disease Tissue Models
2019- NIH Study Section Member ZRG1 CVRS-Q 80: Cardiovascular and Respiratory Sciences NIH Research Enhancement Award Review
2009- American Heart Association's Radiology, Imaging and Surgery Committee
2007- National Science Foundation (NSF)
2016-17 NICHD 3D Printing Study Section (ZHD1 DSR-K(51))
2009-15 NIH Study Section Standing Member ZRG1 VH-D (50, 55) NHBLI System Biology.
2009-10 NIH Study Section Member ZRG1 SBIB-V (58) Challenge Grants Panel 23
2006 National Medical Research Council of Ministry of Health, Singapore

Founder and co-founder:

2018- ValVention, Inc.
2010-18 Folda, LLC
2010-13 WALVE, Inc.

Professional Memberships:

2021 Fellow, American Institute for Medical and Biological Engineering (AIMBE)
2018- Member, Society for Cardiovascular Magnetic Resonance
2016 Fellow, Humboldt Foundation
2014- Member, American Society of Echocardiography
2013- Fellow, American Heart Association
2011- Member, European Mechanics Society
2011- Member, Society of Heart Valve Disease

Consultant:

2014-20 CalHealth, Inc.
2004- Edwards Lifesciences Corp.
2018-19 Cercacor, Inc.
2008-13 Ultrawave Labs, Inc.

Honors

2021 Fellow, American Institute for Medical and Biological Engineering (AIMBE)
2020-22 Fulbright Distinguished Chair in Health Sciences by J. William Fulbright Foreign Scholarship Board
2019 UCI Beall Applied Innovation's inaugural Faculty Innovation Fellow
2016 Fellow, Alexander Humboldt Foundation (experienced researcher fellowship)
2015 American Heart Association Innovative Research Award
2014-20 Member, UCI's Samueli School of Engineering's executive committee
2014-16 Research Committee Member of the American Heart Association, Western States Affiliate.
2013- Fellow, American Heart Association; elected by two Councils on *Cardiovascular Radiology and Intervention* and *Cardiovascular Surgery and Anesthesia* of the American Heart Association.
2012-14 Honorary research fellow, Royal Brompton Hospital, London, UK
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 Transatlantic Career Development Award in Cardiovascular Research from Leducq Foundation
2009 Vivien Thomas Young Investigator Award Finalist nominated by American Heart Association
2002-06 Benjamin M Rosen graduate fellowship in Bioengineering/Engineering Science at Caltech

C. Contributions to Science *(selected from 2 books, 70 peer-reviewed journal publications, 50+ patents/applications, and 125+ conference abstracts and 80+ invited talks)*

1. One major area of focus in my lab is post-processing of cardiac MRI. We have been working on different aspects of cardiac MRI including 4D Flow MRI, artificial intelligence image segmentation and image reconstruction, particularly in congenital heart defects. One of our AI papers (Avendi et al, 2016) has been cited over 613 times since 2016. I have also been awarded a Humboldt fellowship for experienced researchers to study the state of energy in single ventricle anomalies pre- and post-Fontan procedure.

    a. Avendi MR, **Kheradvar A**, Jafarkhani H. A Combined Deep-Learning and Deformable-Model Approach to Fully Automatic Segmentation of the Left Ventricle in Cardiac MRI, *Medical Image Analysis,* 2016 Feb 6;30:108-119. PMID: 28205298
    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. 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;43:1313–1319. (Featured on the cover of the June 2016 issue). PMID: 26584006
    d. Karimi-Bidhendi A., Arafati A., Cheng A., Wu Y., **Kheradvar A.***, Jafarkhani H.* Fully-Automated Deep-Learning Segmentation of Pediatric Cardiac MRI of Patients with Complex Congenital Heart Diseases. *Journal of Cardiovascular Magnetic Resonance*, 2020 Nov 30;22(1):80. doi: 10.1186/s12968-020-00678-0. (*co-corresponding author). PMID: 33256762 PMCID: PMC7706241

2. The other major area of my research is heart valve engineering. My lab has developed three different heart valves through: (1) FoldaValve is a 14-French fully retrievable/repositionable that prevents the leaflets from being stent-crimped; (2) Hybrid Tissue-Engineering Heart Valve (H-TEHV) is a patient-specific tissue engineered valve; (3) AValve is a transcatheter atrioventricular valve system.

    a. Wang DD, Qian Z, Vukicevic M, Engelhardt S, **Kheradvar A**, Zhang C, Little SH, Verjans J, Comaniciu D, O'Neill WW, Vannan MA. 3D Printing, Computational Modeling and Artificial Intelligence for Structural Heart Disease. *Journal of American College of Cardiology: Cardiovascular Imaging*, 2020, Aug 25;S1936-878X(20)30515-5. PMID: 32861647
    b. **Kheradvar A**, Groves EM, and Tseng E. FOLDAVALVE: A Novel 14Fr Totally Repositionable and Retrievable Transcatheter Aortic Valve: Proof of Concept in Sheep. *Euro Interventions*, 2015 Mar 16;10(11) pii: 20141002-01. PMID: 25772904
    c. 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
    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. PMID: 25010918 PMCID: PMC4334568

3. We have been 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 393 times to date. The concept of "vortex formation time index" is currently translated to cardiology clinics and being used by cardiologists for diagnosis of diastolic dysfunctions. My lab has also been a major player in development of echocardiographic Particle Image Velocimetry to map the flow fields inside the heart chambers and vortex imaging is my second major achievement. The journal article describing this method (Kheradvar et al., JASE, 2010) has been cited over 231 times.

    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**, Sahn DJ, Dabiri JO. Optimal vortex formation as an index of cardiac health. *Proceedings of National Academy of Sciences (PNAS)* 2006, 103 (16): 6305-6308. PMID: 16606852
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

4. My research has also significantly contributed to several aspects of cardiovascular solid and fluid biomechanics. For example, we have been the first to characterize the heart valves' collagen fiber orientation and their dynamics in response to the load using second harmonic generation microscopy. In addition, we identified the detrimental effect of stent crimping on the leaflets of the transcatheter heart valves (Alavi et al., 2014), which has been cited 135 times since published.

   a. Zareian R, Tseng JC, Fraser R, Meganck J, Kilduff M, Sarraf M, Dvir D, **Kheradvar A**. Effect of Stent-Crimping on Calcification of Transcatheter Aortic Valves, *Interactive CardioVascular and Thoracic Surgery*, 2019 Jul 1;29(1):64-73. PMID: 30793744 PMCID: PMC6591709
   b. 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: 23180029 PMCID: PMC3963497
   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. Barrett A, Brown JA, Smith MA, Woodward A, Vavalle JP, **Kheradvar A**, Griffith BE, Fogelson AL. A Model of Fluid-Structure and Biochemical Interactions for Applications to Subclinical Leaflet Thrombosis, 2023, *International Journal for Numerical Methods in Biomedical Engineering*; in press.

5. I have been developing heart valves and cardiac imaging modalities. Selected five most relevant patents to the scope of the current project (from 50+ issued (38)/pending U.S. and international patents) are listed:

   a. Avendi MR, Jafarkhani H and **Kheradvar A**. Automated segmentation of organ chambers using deep learning methods from medical imaging; U.S. Patent# 11,182,896
   b. Jafarkhani H, Hajiaghayi M, Groves EM, **Kheradvar A**. Automated 3D reconstruction of the cardiac chambers from MRI or ultrasound, U.S. Patent# 9,875,581.
   c. **Kheradvar A**. Ultrasound-guided delivery system for accurate positioning/repositioning of transcatheter heart valves; U.S. Patent# 11,364,118.
   d. Avendi MR, Jafarkhani H and **Kheradvar A**. Automated segmentation of organ chambers using deep learning methods from medical imaging; U.S. Patent# 10,521,902.

Complete List of my Published Work:
http://www.ncbi.nlm.nih.gov/pubmed/?term=kheradvar+a
https://scholar.google.com/citations?user=7MVET8kAAAAJ&hl=en