

# Biomedical Imaging Research Institute Spring 2020

# Message from the Director



Dear Colleagues and Friends, It has been 10 years since BIRI was established. Thanks to strong commitment and support of the medical center leadership, the tremendous efforts of our amazing BIRI team of faculty, staff, and trainees, and collegiality of all collaborators who share the same passion to translate innovative imaging into clinical significance, we are now an internationally recognized imaging research program that develops innovative and impactful imaging technologies, foster close collaborations with colleagues of various disciplinaries to solve important medical questions, provide state of the art

imaging services to all investigators, and inspire and train future generations of diverse scientists. We have stayed true to our mission and vision.

BIRI had another successful year in every aspect. I am delighted to share some of our recent accomplishments with you. Despite the challenges we currently face in the middle of the COVID-19 pandemic, we have continued to make major research progress while closely following the institutional guidelines to ensure that our workplace is safe for our team and research community. I want to give our team a heartfelt "Thank You" for everything you have done in the last 10 years and during this difficult period. I hope you will be as excited as I am to look forward to what BIRI will bring to medical imaging science and Cedars-Sinai Medical Center in the next 10 years! - Debiao Li, PhD

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### The First Group of Students were awarded in Master of Science in Magnetic **Resonance in Medicine**

The first five graduate students: Taylor Coss, John Van Dyke, Daniah Al Amili, Fardad Michael Serry, and Cody Lynch, from Biomedical Research Institute were awarded master's degree in Magnetic Resonance in Medicine. They were part of the largest graduating class since Cedars-Sinai Graduate school of Biomedical Sciences held its first commencement in 2013.

The 20-month accredited degree program consists of didactic courses, laboratory and clinical rotations along with an opportunity to rotate with industry imaging scientists. Master's students are required to hold a defense of their thesis at the end of their study. All five graduates joined BIRI graduate program in 2017 and completed their program in 2019 with the following thesis titles:

Taylor Coss: "Automated Detection and Segmentation of Tumors in Breast Cancer for MRI" Thesis Advisor: Dr. Touseef Ahmad Qureshi

John Van Dyke: "Deep Learning methods for analysis of myocardial perfusion MRI datasets" Thesis advisor: Dr. Behzad Sharif

Daniah Al Amili: "Quantification comparison of PET/CT and PET/MR in oncology with novel measures of PET uptake" Thesis Advisor: Dr. Damini Dey

Fardad Michael Serry: "Phased array image reconstruction and noise characterization for the prototype Unified Coil system" Thesis advisor: Dr. Hui Han

Cody Lynch: "Differential Characteristics in the Substantia Nigra Pars Compacta of Parkinson's Disease Patients on Neuromelanin-Sensitive MRI" Thesis advisor: Dr. Zhaoyang Fan



First group of graduates of the Master's program, program directors, and Medical Center leaders.



# **Department Highlights**

## AI and Deep Learning

### Machine learning ischemia risk by integrating stenosis and plaque from coronary CT Angiography



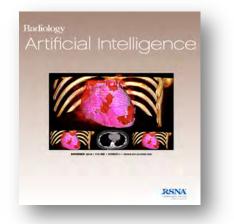
Most heart attacks occur due to coronary plaque rupture at sites without prior severe narrowing or stenosis of the coronary artery. A study team led by BIRI investigator Dr. Damini Dey has developed a noninvasive machine learning ischemia risk score for each vessel, combining coronary stenosis and plaque quantified from coronary CT Angiography (CTA).

Damini Dey, PhD.

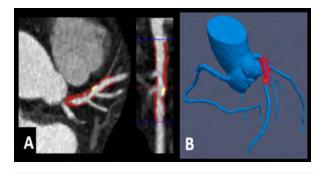
A study team led by BIRI investigator Dr. Damini Dey has developed a noninvasive machine learning ischemia risk score for each vessel, combining coronary stenosis and plaque quantified from coronary CT Angiography (CTA). The ischemia risk score was validated in the multicenter NXT clinical trial, in which 284 patients underwent coronary CTA invasive coronary angiography with Fractional Flow Reserve (FFR); this paper has been published in European Radiology. These findings could help stratify patients as low or high-risk following CTA and indicate which patient may benefit from further noninvasive ischemia testing, noninvasive FFR or FFR assessment.

Coronary plaque features can be non-invasively evaluated from coronary CT Angiography, which is increasingly used as a diagnostic test for the assessment of the coronary arteries. Over the last several years, Dr. Dey has led the development and validation of new methods for standardized, semiautomated measurement and characterization of coronary plaque (Figure 1), which has been shown to correlate highly with invasive intravascular ultrasound. The software tool Autoplaque is now used for clinical research in over 35 clinical sites; coronary plaque characterization has been shown to predict ischemia as well as prognosis.

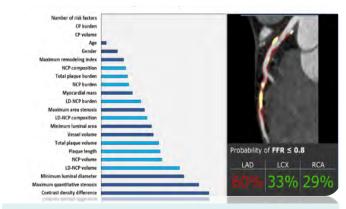
Quantitative image analysis yields an ensemble of imaging biomarkers, which need to be considered by the physician together with clinical information for the final diagnosis. Currently this process is highly subjective and not optimized. Dr. Dey's team has applied machine learning to objectively combine imaging biomarkers measured from coronary CTA into a single continuous risk score to predict ischemia (Figure 2).



Front cover of Radiology AI featuring Dr. Dey's paper on deep learning quantification of epicardial fat from cardiac CT



**Figure 1.** Standardized quantification of plaque lesion in proximal to mid LAD artery. (A) Left panel shows transverse and right panel shows straightened view (red-NCP; yellow-CP). (B) 3D rendering of the coronary tree with plaque lesion



**Figure 2.** Left panel: Imaging biomarkers with information gain ranking > 0.001 for ischemia were combined to form the ischemia risk score. Right panel: Left anterior descending artery of an unseen 67year old symptomatic male patient undergoing CTA, along with the integrated machine learning ischemia risk score (60%). Invasive FFR in the LAD Artery was reduced (0.73), indicating ischemia



# **BIRI Research Making an Impact**

### Detecting Heart Disease with Needle-Free MRI

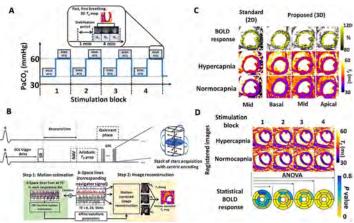




Randy Yang, PhD.

Rohan Dharmakumar, PhD

A study team led by BIR has developed an advanced type of MRI for detecting how the heart is using oxygen. The findings in experimental models, confirmed in humans, could lead to a new noninvasive way to diagnose ischemic heart disease - the leading cause of death in U.S.- and help enable earlier intervention. Ischemic heart disease, also known as coronary heart disease, occurs when the heart's arteries cannot deliver enough oxygen-rich blood to the heart. The condition results from the buildup of waxy plaque inside the coronary arteries that can narrow or block them. Patients often do not know they have the disease until complications, such as a heart attack, develop. Early detection of ischemic heart disease could prevent many deaths, according to Rohan Dharmakumar, PhD, Associate director of the Cedars-Sinai Biomedical Imaging Research Institute and senior author of the study published in the journal Science Translational Medicine. But current detection methods are either invasive, time-consuming or require various drugs, he explained. The most widely used methods rely on imaging technologies to measure blood flow to the heart muscle under different conditions. They may entail exercise stress that more than half of patients cannot tolerate, injections of contrast agents that are contraindicated for chronic kidney disease patients or radioactive tracers that pose incremental risk to patients. Due to variations among individuals and other technical challenges, these tests also may not provide a full picture of the extent and severity of disease, Dr. Dharmakumar explained. "There is an important need for an accurate, noninvasive way to measure oxygenation of the heart muscle that can be applied across populations," he said.



Cardiac fMRI framework integrating MRI, hypercapnic stimulation, and statistical analysis.

(A) Data acquisition framework: The approach used to acquire 3D MRI under periodic changes in PaCO2 (normocapnic and hypercapnic conditions), preceded by a short delay (stabilization period) to ensure that the acquisitions are only triggered once the desired PaCO2 values are reached.

(B) Time-efficient, free-breathing, confounder-corrected whole-heart *T*2 mapping. Left: The timing diagram shows a *T*2 preparation scheme composed of composite adiabatic RF pulses and spoiled GRE readout, used to minimize *B1* and *B0* artifacts at 3 T. An SR preparation was added to eliminate the signal dependence on heart rate between segmented readouts, and navigator (NAV) pulses were added to minior the respiratory motion during acquisition. Right: The centric-encoding scheme with hybrid trajectory to ensure optimal *T*2 weighting. Bottom: motion-correction algorithm and *T*2 mapping.

(C) 3D myocardial BOLD response: 3D 72 maps (basal, midventricular, and apical) acquired during normocapnia and hypercapnia (single stimulation block). For reference, results from 2D imaging obtained from a midventricular slice are also shown (left column). BOLD response was computed as ((hypercapnic myocardial *T2*)/(normocapnia myocardial *T2*)) × 100%.

(D) Statistical framework: A schematic of the statistical framework using repeated-measures one-way ANOVA to discriminate between registered images of myocardial segments that are or are not statistically responsive, based on the hypothesis testing outlined in text, after each repeat hypercapnic/normocapnic stimulation. The polar maps on the lower row show the AHA segmentation with *P* values assigned on the statistical test.

To address this need, the investigative team, drawn from multiple institutions, developed a new testing method called cardiac functional MRI. It uses a breathing machine that changes the concentration of carbon dioxide in the blood. Normal blood vessels in the heart respond to these changes by efficiently adjusting blood flow to provide more or less oxygen. Diseased blood vessels do not. By imaging the heart while changing the carbon dioxide concentrations in the blood, the investigators showed they could accurately detect inadequate oxygenation of the heart muscle and map regions of the heart disease. "Although our findings in this study are limited to experimental models, we anticipate that our proposed cardiac functional MRI approach would translate well in humans," said Dr. Dharmakumar, professor of Biomedical Sciences. He said his team is developing imaging and gas-control strategies to translate the new technology for use in patients with ischemic heart disease, with a goal of making it available in the clinic within five years. In addition to studying coronary artery disease, the new method potentially could be useful for evaluating other cases where heart blood flow is affected, such as a heart attack or injury to the heart from cancer treatment, according to Hsin-Jung (Randy) Yang, PhD, a project scientist in Dharmakumar's laboratory and the study's first author.



# **BIRI Research Making an Impact**

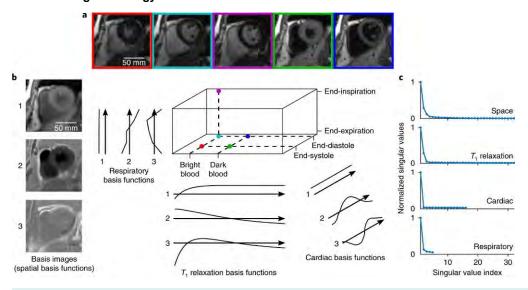
### Multitasking Approach To Revolutionize MR Imaging



Debiao Li. PhD Anthony Christodoulou. PhD

Quantitative MRI is typically very time consuming and difficult to perform. Each parameter is typically measured from its own series of images, so measuring multiple parameters leads to long, inefficient scanning sessions. Furthermore, cardiac and breathing motion creates misalignment between images, causing additional problems. The standard approach to motion is to either remove it (e.g., ask the patient to hold their breath) or to synchronize image acquisition with it (e.g., using

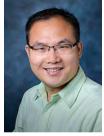
electrocardiography (ECG) to monitor cardiac motion). This makes scan times even longer, limits imaging to patients who can repeatedly perform long breath holds (which is difficult for aging or weak patients) and who have predictable cardiac motion (which is not true of patients with cardiac arrhythmias). Furthermore, these methods are often unreliable and difficult to perform. BIRI researchers Dr. Debiao Li and Dr. Anthony Christodoulou recently received a 4-year grant from the National Institute of Biomedical Imaging and Bioengineering, National Institutes of Health to develop and validate a one-stop, push-button solution for comprehensive, motion-resolved quantitative magnetic resonance imaging (MRI) using their MR Multitasking technology.



**a**, Locations of different images in a space with 3 time dimensions. Different  $T_1$  weightings lie along the inversion time axis (horizontal), different cardiac phases lie along the cardiac time axis (depth) and different respiratory phases lie along the respiratory time axis (vertical). **b**, The three most significant basis functions describing each dimension of the image tensor, as reconstructed from 1 min worth of data. **c**, Singular value curves from the higher-order SVD of 12.3 min worth of raw subspace training data (that is, enough data to cover all motion-state and contrast combinations), demonstrating that the singular values decay quickly for all unfoldings of the raw data tensor.

MR Multitasking, on the other hand, redesigns quantitative MRI around the concept of images as functions of many time dimensions, each corresponding to a different dynamic process, and then uses mathematical models known as low-rank tensors to perform fast, multidimensional imaging. This allows continuous acquisition of imaging data even while the subject is moving, providing motion-resolved parameter maps without breath holding or motion synchronization. Multitasking makes it possible to measure multiple tissue biomarkers in a single scan, even in moving organs, and is both comfortable for patients and simple for technologists to perform. The technology resulting from this project will be applicable to any organ system, offering clinicians and investigators a valuable tool to diagnose, monitor, and study a wide range of diseases.

### Studying Brain Development of Drug Exposed Infants



Wei Gao, PhD.

Dr. Wei Gao established a multi-site team with scientists from Cedars Sinai, UCLA and Tarzana Treatment Center to chart the growth trajectories of both drug-fee and drug-exposed babies during the first 10 years of life. This is one of NIH's unprecedented initiatives to understand the development of infant brains. NIH's HEAL initiative entitled **HEALthy Brain and Child Development Study (HEALthy BCD)** granted an award to conduct the planning study. This planning phase will hopefully pave the way for the next phase of 10-year study involving recruiting, scanning, and longitudinally following hundreds of babies from fetal period to 9 years of age at Cedars. Nationwide there will be >10k mother-baby dyads involved as a multi-site study. Through this award and working with other teams across the nation, they aim to gain a better understanding of how prenatal drug exposure may impact offspring brain and behavioral development thus better informing intervention practices and public policy making.





### Conferences

#### BIRI @ SCMR Annual Scientific Session 2019

BIRI investigators had a highly successful meeting at the 22nd Annual Scientific Sessions of the Society for Cardiovascular Magnetic Resonance which was held February 6-9, 2019 in Bellevue, WA. We had many presentations and received several awards and distinctions. Highlights include:

#### Awards and Honors:

SCMR Early Career Award Winner: Hsin-Jung (Randy) Yang, PhD Runner up for SCMR Early Career Award: Transitional Science- Eric Johnson, MS Clinical Science- Guan Wang, PhD

#### **Presentations:**

Yang H, Liu W, Stager J, Xie Y, Selvin S, Azab L, Dong Q, She N, Handelin R, Jiang T, Serry M, Dharmakumar R, Li D, Han H.

"Overcoming Off-Resonance Limitations in High Field CMR with High-Order Local Whole Heart B0 Shimming Using a UNIfied shim-RF Coil (UNIC)", Society of Cardiovascular Magnetic Resonance, 2019 (oral presentation).

#### BIRI @ ISMRM Conference 2019

BIRI investigators attended the ISMR 27<sup>th</sup> annual meeting and exhibition which was held in Montreal, QC, Canada. We had many presentations. Highlights include:

#### **Presentations:**

#### Christodoulou A, Wang N, Shaw J, Bi X, Xie Y, Nguyen C, Li D.

"Respiratory motion compensated Multitasking for 3D myocardial perfusion without breathholds, ECG, or multiple boluses". International Society for Magnetic Resonance in Medicine, 2019; #1175 (oral presentation).

# Wang N, Christodoulou A, Gaddam S, Wang L, Xie Y, Deng Z, Zhou Z, Yang W, Fan Z, Tuli R, Lo S, Hendifar A, Pandol S, Li D.

"Whole-abdomen Free-breathing Quantitative Dynamic Contrast Enhanced (DCE) MR Imaging of Pancreatic Ductal Adenocarcinoma (PDAC) with Fast T1 Mapping Using Multitasking: A Pilot Study". International Society for Magnetic Resonance in Medicine, 2019; #0638 (oral presentation).

# Wang L, Xie Y, Gaddam S, Wang N, Deng Z, Zhou Z, Yang W, Fan Z, Jiang T, Lo S, Hendifar A, Pandol S, and Li D.

"Non-Contrast Multiparametric Mapping for Pancreatic Ductal Adenocarcinoma Cancer (PDAC) Tissue Characterization". International Society for Magnetic Resonance in Medicine, 2019; #0587.

#### Ma S, Christodoulou A, Nguyen C, Han F, Wang N, Xie Y, Li D.

"Three-Dimensional Whole Brain Simultaneous T1, T2, and Apparent Diffusion Coefficient Mapping Using MR Multitasking". International Society for Magnetic Resonance in Medicine, 2019; #0308 (oral presentation).

#### BIRI @ SMRA Conference 2019

BIRI investigators attended the 31st Annual International Conference of the Society for Magnetic Resonance Angiography which was held August 27-30, 2019 in Nantes, France. We had many presentations. Highlights include:

#### **Presentations:**

#### Xie Y, Chen Y, Yang Q, Yan C, Christodoulou A, Li D.

"Towards Single Breath-Hold Whole-Heart Coronary MRA Via Cross-Domain Deep Learning", Society for Magnetic Resonance Angiography, 2019; #679987 (oral presentation).

#### Christodoulou A, Wang N, Shaw J, Bi X, Xie Y, Nguyen C, Li D.

"Single-bolus quantitative 3D myocardial perfusion imaging without breath holds or ECG gating via respiratory-compensated MR Multitasking", Society for Magnetic Resonance Angiography, 2019; #679987 (oral presentation).



#### Cedars Sinai | Biomedical Imaging Research Institute Newsletter | Spring 2020 cedars-sinai.org/research/departments-institutes/biomedical-imaging.html

# SCMR 22ND ANNUAL SCIENTIFIC SESSIONS

Global CMR: Innovation and Clinical Outcomes

February 6 - 9, 2019 Bellevue, WA USA





Cedars Sinai | Biomedical Imaging Research Institute Newsletter | Spring 2020 cedars-sinai.org/research/departments-institutes/biomedical-imaging.html

### Conferences

#### BIRI @ AHA Conference 2019

Dr. Dey gave a talk for the opening session at the American Heart association conference in Philadelphia. Her talk focused on AI for cardiovascular imaging with many great examples of how we apply artificial intelligence to machine learning.

#### BIRI @ SCMR Annual Scientific Sessions 2020

BIRI investigators attended the 23<sup>rd</sup> Annual Scientific Sessions of the Society for Cardiovascular Magnetic Resonance which was held February 12-15, 2020 in Orlando, FL. We had many presentations and received several nominations for early career award. Highlights include:

#### Awards and Honors:

Early Career Award Finalists: Basic Science - Xingmin (Diane) Guan, MS Zhehao Hu

#### Presentations:

Christodoulou A "Multidimensional CMR: Why not just capture everything?", 2020; (invited talk).

#### Wang N, Cho I, Chung M, Lu M, Christodoulou A, Li D, Chang HJ, Xie Y.

"Quantitative Multi-contrast Atherosclerosis Characterization (qMATCH) of Atherosclerosis: Initial Study on Plaque Analysis", 2020; #:749492 (moderated e-poster).

#### Hu Z, Christodoulou A, Wang N, Song S, Maya M, Ishimori M, Forbess L, Xiao J, Bi X, Han F, Li D,

**Fan Z.** "Development of an MR Multitasking-based Multi-dimensional Assessment of Cardiovascular System Technique: Feasibility on the Thoracic Aorta", 2020; #750771 (oral ECA presentation).

#### Guan X, Zhang X, Sykes J, Butler J, Tang R, Yang HJ, Prato F, Dharmakumar R.

"Image Contrast Loss in Double Inversion Recovery Dark-blood T2\* CMR of Intramyocardial Hemorrhage 2020; #751247 (oral ECA presentation).

#### Johnson E, Nair A, Cokic I, Yang HJ, Kumar A, Dharmakumar R.

"Impaired Rest Perfusion in Iron-Laden Myocardial Infarct Regions with Histological Insights", 2020, (oral presentation).

#### Yang HJ, Oksuz I, Dey D, Sykes J, Klein M, Butler J, Kovacs M, Sobczyk O,

Cokic I, Ślomka P, Bl X 6, Li D, Tighiouart M, Tsaftaris S, Prato F, Fisher J, Dharmakumar R. "Reliable Noncontrast Myocardial Ischemia Detection Using Cardiac fMRI (cfMRI)", 2020; #751334 (poster).

#### Y Chen, Guan X, Yang HJ, Tang R, Cokic I, Dharmakumar R

"Quantification of Hemorrhagic Myocardial Infarctions with T2\* CMR at 1.5T and 3.0T", 2020; #751298 (poster).

#### Youssef K, Beaulieu T, Cheema K, Dyke J, Dharmakumar R, Sharif B.

"Deep Learning for High-resolution Myocardial Blood Flow Mapping: Rapid Automated Post-Processing with Robustness to Noise and Motion", 2020; #749050 (poster).

#### Han P, Zhang R, Wagner S, Xie Y, Cingolani E, Marban E, Christodolou AG, Li D

"ECG-free myocardial T1/ECV mapping in small animals at high heart rates using MR Multitasking: A feasibility study in a HFpEF rat model", 2020; #749761 (quick fire oral and poster).

#### Y Chen, Kwan A, Yang Q, Yan C, Christodoulou A, Chan HJ, Li D, Xie Y.

"Super-Resolution Coronary MRA by Joint Deep Learning: Initial Diagnostic Analysis", 2020; #749298

### Key Scientific Meetings in 2020/21









SCMR 23rd Annual Scientific Sessions Transforming Cardiovascular Care Through Discoveries in Imaging February 12 - 15, 2020 Orlando, FL USA

Scientific Sessions

Nov. 16-18, 2019 | Philadelphia, PA

#44419





Society for MR Angiography



American American Heart Association (AHA Heart Scientific Sessions Association, November 14-16, 2020 Dallas, TX

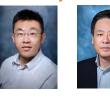


Society for Cardiovascular Magnetic Resonance April 8-9 2021 London, UK



# FY 2020 Highlights

#### **Recently Awarded Grants**



Hui Han, PhD and Debiao Li, PhD. Whole – brain spectroscopic MRI for radiation treatment planning (NIH UO1)



**Chaoyang Fan, PhD and Wensha Yang, PhD** Novel Four Dimensional Magnetic Resonance Imaging to Monitor Pancreatic Tumor Infiltrating Blood Vessels and Tumor Response to Chemoradiation Therapy (NIH R21)



Zhaoyang Fan, PhD Longitudinal and quantitative MR Plaque Imaging for Prediction of Response to Medical Management in Symptomatic Intracranial Atherosclerosis (NIH R01)



Anthony Christodoulou, PhD and Debiao Li, PhD Motion-Resolved, Comprehensive Quantitative Tissue Characterization Using MR Multitasking (NIH R01)



#### Wei Gao, PhD

Effects of maternal obesity and inflammation on offspring brain development (subcontract to NIH 1R01)

Wei Gao, PhD

Parsing early emerging heterogeneity related to autism spectrum disorder (subcontract to NIH RO1)

#### Wei Gao, PhD

Planning Phase for the Healthy Baby and Child Development Study in Los Angeles County Area (NIH R34)



#### Rohan Dharmakumar, PhD

Mechanistic Insights to a Translatable Therapy for Acute Reperfused Hemorrhagic Myocardial Infarctions (NIH 1R01)

#### Rohan Dharmakumar, PhD

Accurate, Needle-Free, MRI-based Detection of Ischemic Heart Disease without Contrast Agents (NIH R01)

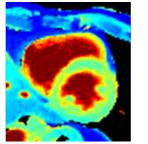


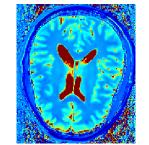
#### Damini Dey, PhD

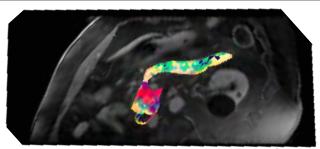
Integrated prediction of cardiovascular events by automated coronary plaque and pericoronary adipose tissue quantification from CT Angiography (NIH R01)

#### **Publications with Impact Factor of >10**

- Dey D, Slomka PJ, Leeson P, Comaniciu D, Shrestha S, Sengupta PP, Marwick TH. Artificial Intelligence in Cardiovascular Imaging: JACC State-of-the-Art Review. J Am Coll Cardiol. 2019 Mar 26;73(11):1317-1335.
- Williams MC, Kwiecinski J, Doris M, McElhinney P, D'Souza MS, Cadet S, Adamson PD, Moss AJ, Alam S, Hunter A, Shah ASV, Mills NL, Pawade T, Wang C, McCall JW, Bonnici-Mallia M, Murrills C, Roditi G, van Beek EJR, Shaw LJ, Nicol ED, Berman D, Slomka PJ, Newby DE. Dweck MR, Dey D. Lowattenuation non-calcified plaque on coronary CT angiography predicts myocardial infarction *Results from the multicenter SCOT-HEART trial*. Circulation 2020;141:1452-1462.
- Ibanez B, Aletras AH, Arai AE, Arheden, H, Bax J, Berry C, Bucciarelli-Ducci C, Croisille P, Dall'Armellina E, Dharmakumar R, Eitel I, Fernández-Jiménez R, Friedrich MG, García-Dorado D, Hausenloy DJ, Kim R, Kozerke S, Kramer CM, Salerno M, Sánchez-González J, Sanz J, Fuster V. Cardiac MR Endpoints in Myocardial Infarction Experimental and Clinical Trials. JACC State-of-the-Art Review by JACC Scientific Expert Panel. JACC. 2019 Jul 16;74(2):238-256
- Mishra R, Haldar S, Placencio V, Madhav A, Rohena-Rivera K, Agarwal P, Duong F, Angara B, Tripathi M, Liu Z, Gottlieb RA, Wagner S, Posadas EM, Bhowmick NA. "Stromal epigenetic alterations drive metabolic and neuroendocrine prostate cancer reprogramming. J. Of Clinical Investigation 2018 Oct 1;128(10):4472-4484
- Wei J, Nelson M, Sharif B, Shufelt C, Bairey Merz CN. Why Do We Care About Coronary Microvascular Dysfunction and Heart Failure with Preserved Ejection Fraction: Addressing Knowledge Gaps for Evidence-based Guidelines. European Heart Journal 2018;39(37):3451-3
- Yang HJ, Ilkary O, Dey D, Šykes J, Klein M, Butler J, Kovacs MS, Sobczyk O, Cokic I, Slomka P, Bi X, Li D, Tighiouart M, Prato FS, Tsaftaris SA, Fisher JA, Dharmakumar R. Accurate Needle-Free Assessment of Myocardial Oxygenation for Ischemic Heart Disease. Science Translational Medicine. 2019 May 29;11(494)







Future of MRI Developed at Cedars: Motion-resolved virtual pathology (color images for tissue characterization)



# **Department Acknowledgments**

### Master's Program Student Spotlight



**Taylor Beaulieu** graduated from the University of California, Riverside with a Bachelor's Degree in Physics in 2018. He is currently finishing his Master's Degree in the Cedars-Sinai's MSMRM program. Following his Master's studies he will begin attending UCLA this Fall to work towards his PhD degree in Bioengineering under the mentorship of Dr.Behzad Sharif, with a focus on cardiovascular MRI and signal processing. His primary research interests include developing deep learning and advanced machine learning tools to improve the robustness and accuracy of myocardial blood flow mapping with MRI.

**Project Summary**: With coronary artery disease (CAD) as one of the leading causes of Death in the United States, there is a tremendous demand for non-invasive imaging techniques to help identify early and subclinical stages of CAD. Magnetic resonance imaging (MRI) has several advantages in this regard hence putting it in a prime position to meet this demand including its excellent soft tissue contrast, and lack of ionizing radiation. Cardiac MRI has emerged as one of the leading techniques for the assessment of myocardial function and viability. However, for high-resolution assessment of myocardial blood flow, there are still roadblocks preventing a fast and fully-automated quantitative analysis approach of MRI datasets.

Taylor's Master's thesis, which is being conducted in Dr. Sharif's research lab (Laboratory for Translational Imaging of Microcirculation), is focused on developing and testing an Artificial Intelligence-based approach to automatically segment the myocardium in a dynamic series of T1-weighted MR images acquired during the first-pass of a gadolinium-based contrast agent. Obtaining accurate image segmentations is currently the most time-consuming portion of quantitative blood flow analysis; therefore, the ability to quickly and accurately segment the dynamic contrast-enhanced images would allow for a much more robust and observer-independent quantification of myocardial blood flow.

**Expected Outcomes**: Taylor's contributions are expected to help the development and testing of a fully automated software, capable of performing rapid end-to-end quantitative myocardial blood flow analysis. He is also working on improving accuracy and generalizability of the deep earning models to different MRI scanner platforms. Fast and accurate quantitative analysis will

hopefully push quantitative CMR perfusion imaging towards being more robust and clinically viable.



Karandeep Cheema graduated from Oregon State University with a Bachelor of Science in Physics in 2017. His passion to use physics practically inspired him to join the master's program in magnetic resonance and imaging at Cedars-Sinai. He is excited to work with known experts in the field and use the stateof-the-art equipment to help image the body and develop novel imaging techniques. During his Master's studies he worked in Dr. Behzad Sharif's lab and focused on the

application of artificial intelligence (AI) tools for analysis of cardiac perfusion MRI data. After finishing his master's program, he will enroll as a PhD student at UCLA and work with Dr. Debiao Li in the bioengineering department. His ultimate goal is to work with Siemens as a project scientist in the R&D department.

**Project Summary**: Almost half of the patients who undergo diagnostic procedures to detect coronary artery disease end up having a normal test. A large portion of these patients suffer from ischemic heart disease due to "small vessel" coronary disease. Dr. Sharif's lab is currently working towards developing and validating high-resolution quantitative myocardial perfusion techniques to enable reliable and accurate characterization of patients with small-vessel coronary dysfunction. Under the mentorship of Dr. Sharif, Karandeep is applying AI tools to quantify myocardial blood flow from dynamic contrast-enhanced perfusion datasets and to test the feasibility of a complete "end to end" automatic quantification approach, which has the potential to be used for rapid assessment of patients with suspected small-vessel coronary dysfunction.

**Expected Outcomes:** Karandeep's contribution to this ongoing project would eventually result in the development of a software package capable of performing rapid myocardial perfusion quantification with robustness to noise, which has the potential to improve the objective diagnosis of small-vessel coronary disease.

# **Notable Mentions**



Congratulations to **Damini Dey, PhD.**, she will serve as member of the Cancer, Heart and Sleep Epidemiology B Study Section, Center for Scientific Review beginning July 1, 2020. Her contributions to the National Health Institute (NIH) are of great value to the medical and allied research in this country.



Hsin-Jung "Randy" Yang, PhD. receives the SCMR Early Career Award



Congratulations to **Debiao Li, PhD.**, who was elected as a Fellow, International Academy of Medial and Biological Engineering in 2019. The International Academy of Medical and Biological Engineering (IAMBE) is made up of fellows who are recognized for their outstanding contributions to the profession of medical and biological engineering.



Congratulations to **Randy Yang**, PhD. for receiving the SCMR Early Career Award at the SCMR conference held in Bellevue, WA from February 6-9, 2019. His talk on - *Mapping Myocardial Oxygenation Reactivity with Highly Time-Resolved Beat-by-Beat, Free-breathing, Ungated T2 CMR at 3T* was recognized as the best talk in the "Basic Science Oral Abstract" category; an honor well deserved!

Congratulations to Daniel Berman, MD, for a successful 35<sup>th</sup> Annual Case Review with the Experts. The symposium held on January 17-19, 2020 featured the most updated practical training in case interpretation, reporting and medical decision making from leading clinicians and scientists in cardiac imaging, including several of our BIRI faculty: Damini Dey, PhD, Rohan Dharmakumar, Phd, Anthony Christodoulou, PhD, and Balaji Tamarappoo, MD, PhD



### **Department Acknowledgments**

# Welcome to our Institute!



Gloria Arrenquin Research Operations Associate

Rachel Marcus

**Clinical Research** 

Associate I

Irene Lee

**MRI** Technologist

Yinyin Chen, MD, PhD

Postdoctoral Scientist



Hsu-Lei Lee, PhD MR Physicist



Xianglun "Vincent" Mao, PhD Postdoctoral Scientist



Nuclear Medicine Technologist



Khalid Youssef, PhD Project Scientist



Janelle Liu, PhD Postdoctoral Scientist



Erin Gallent, MD, PhD Visiting Postdoctoral Scientist



Clinical Research Coordinator II



Ting Liu, MD, PhD Postdoctoral Scientist



Chaowei Wu Visiting Graduate Student



**Qiuju Hu, MD** Visiting Postdoctoral Scientist



Zihao Chen Visiting Graduate Student



Visiting Graduate Student



Natalin Aroyan Administrative Assistant



Anand Nair, PhD Project Scientist



Junzhou Chen Visiting Graduate Student



Dilek Yalcinkaya Visiting Graduate Student



Andrew Howarth, MD, PhD Visiting Faulty

### Acknowledgment for Grant Dagliyan and Joceline Mota

On behalf of all of BIRI, we want to thank Grant Dagliyan, DRSc, MS, MPH and Joceline Mota, MS for all of their hard work and dedication throughout the duration of their time with the department. They have both been dedicated and valued employees for BIRI and have made a profound impact within the department.

Grant has facilitated numerous programs and projects for BIRI and we would like to congratulate his transfer to the Cancer Center acting as the Manager of Research Operations for Strategic Initiatives and Alliance Development. He will still have some efforts within BIRI for his high valued projects that are ongoing. Joceline has provided exceptional support for BIRI's faculty and staff. We are excited for her continued growth and success within Cedars-Sinai and wish to congratulate her on her new role in the Cancer Center as a Program Administrator for Strategic Initiative and Alliance Development.

We wish you both all the best on your future endeavors and we look forward to hearing what you both continue to accomplish!



### **BIRI Updates**

### **BIRI Open House was a Major Success!**



#### Dr. Han's Lab Move

MRI Hardware Laboratory has moved most of its operations to the 5<sup>th</sup> floor of the Pacific Design Center, (*the Green Building, room G-521*). This room is adjacent to but separate from the much larger area housing the Graduate Education Center, Cancer Research Center, and Biostatistics Core.

The MR Hardware Engineering group's new laboratory space houses BIRI's newly acquired instructional NMR system, RAISED 3D printer, and other equipment for designing, prototyping, and testing of MR hardware, including a dedicated area for radio-frequency hardware used in MR coil arrays. We have several projects involving hardware and software, and welcome inquiries into participation.

The spacious MRI hardware lab in PDC will provide a conducive environment to expand our team. This will facilitate the development of the new-gen MRI coil systems. We have pioneered novel combined shim-RF coil concept that has been adopted by many groups worldwide. The new-gen coil technology will tackle one of the major challenges in imaging—variability of anatomies and physiologies among different patient populations—and pave the way for precision medicine with MRI.



Office space for MRI Hardware Laboratory housed in the Pacific Design Center



Annual BIRI Holiday Party: Food, fun, raffles, white elephant and ugly sweater contest were some of the highlights of this annual tradition.



BIRI beach volleyball to welcome the new UCLA cohort.

#### **Contact Us**

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The NIH Bioengineering Research Partnership (BRP) U01 meeting was hosted by BIRI at Cedars-Sinai this year. The meeting discussed the latest development about a multi-interdisciplinary and multi-institutional collaboration project. The project involves novel hardware development about new gen. MRI head coil by Dr. Han's team, rapid and motion-robust sMRI method by Dr. Andrew Maudsley's team, and new clinician-friendly web-based interface by Dr. Hyunsuk shim's team. The combined efforts are to produce tools and methods needed for widespread clinical adoption of spectroscopic MRI for the clinical management of brain cancer.

From left to right: Mohammed Goryawala (Miami), Andrew Maudsley (Miami), Sulaiman Sheriff (Miami), Hyunsuk Shim (Emory), me, Karthik Ramesh (Emory), Zander Giuffrida (Emory)



### **Recent Publications**

Biomedical Imaging Research Institute members published over 120 original manuscripts and reviews in the past year. Research Imaging Core (RIC) users have published over 150 manuscripts using RIC data. Recent highlighted publications include:

Imaging structural and functional brain development in early childhood. Gilmore JH, Knickmeyer RC, Gao W. Nature Reviews Neuroscience. Impact factor: 33.162.

A review on neuroimaging studies of genetic and environmental influences on early brain development. Gao W, Grewen K, Knickmeyer RC, Qiu A, Salzwedel A, Lin W, Gilmore JH. 2019. Neuroimage 185:802-812.

Gut microbiome and brain functional connectivity in infants-a preliminary study focusing on the amygdala. Gao W, Salzwedel AP, Carlson AL, Xia K, Azcarate-Peril MA, Styner MA, Thompson AL, Geng X, Goldman BD, Gilmore JH, Knickmeyer RC. 2019. Psychopharmacology 236:1641-1651.

The UNC/UMN Baby Connectome Project (BCP): An overview of the study design and protocol development. Howell BR, Styner MA, Gao W, Yap PT, Wang L, Baluyot K, Yacoub E, Chen G, Potts T, Salzwedel A, Li G, Gilmore JH, Piven J, Smith JK, Shen D, Ugurbil K, Zhu H, Lin W, Elison JT. 2019. Neuroimage 185:891-905.

Development of Amygdala Functional Connectivity During Infancy and Its Relationship With 4-Year Behavioral Outcomes. Salzwedel AP, Stephens RL, Goldman BD, Lin W, Gilmore JH, Gao W. 2019. Biological psychiatry Cognitive neuroscience and neuroimaging 4:62-71.

"Quantitative 3D dynamic contrast enhanced (DCE) MR imaging of carotid vessel wall by fast T1 mapping using multitasking," N. Wang, A. G. Christodoulou, Y. Xie, Z. Wang, Z. Deng, B. Zhou, S. Lee, Z. Fan, H. Chang, W. Yu, D. Li, Magn Reson Med, vol. 81, no. 4, pp. 2302–2314, Apr 2019.

"Free-breathing, non- ECG, continuous myocardial T1 mapping with CMR multitasking," J. L. Shaw, Q. Yang, Z. Zhou, Z. Deng, C. Nguyen, D. Li, A. G. Christodoulou, Magn Reson Med, vol. 81, no. 4, pp. 2460–2463, Apr 2019.

In Vivo Imaging of Therapeutic Stem Cells in Tendon Regeneration via Superparamagnetic Iron Oxide Particles. Bez M, Sheyn D, Ben David S, Da X, Tawackoli W, Wagner S, Gazit D, Pelled G. The American Journal of Sports Medicine, Accepted.

Transient Brachyury Activity Initiates Primitive Streak Mesodermal Cells toward a Notochordal Fate. Sheyn D, Ben-David S, Tawackoli W, Zhou Z, Salehi K, Bez M, De Mel S, Chan V, Giaconi J, Yameen H, Hazanov L, Seliktar D, Li D, Gazit D, Gazit Z. Theranostics, Accepted.

Bone-Chip System to Monitor Osteogenic Differentiation using Optical Imaging. Sheyn D, Cohn Yakubovich D, Ben-David S, De Mel S, Chan V, Hinojosa C, Wen N, Hamilton GA, Gazit D, Gazit Z. Microfluidics and Nanofluidics, Accepted.

The Influence of Polymer Blends on Regulating Chondrogenesis. Bherwani A, Chang CC, Pelled G, Gazit Z, Gazit D, Rafailovich M, Simon M. Coatings, Accepted.

Accurate Needle-Free Assessment of Myocardial Oxygenation for Ischemic Heart Disease. Yang HJ, Ilkary O, Dey D, Sykes J, Klein M, Butler J, Kovacs MS, Sobczyk O, Cokic I, Slomka P, Bi X, Li D, Tighiouart M, Prato FS, Tsaftaris SA, Fisher JA, Dharmakumar R.Science Translational Medicine. 2019 May 29;11(494)

Cardiac MR Endpoints in Myocardial Infarction Experimental and Clinical Trials. Ibanez B, Aletras AH, Arai AE, Arheden, H, Bax J, Berry C, Bucciarelli-Ducci C, Croisille P, Dall'Armellina E, Dharmakumar R, Eitel I, Fernández-Jiménez R, Friedrich MG, García-Dorado D, Hausenloy DJ, Kim R, Kozerke S, Kramer CM, Salerno M, Sánchez-González J, Sanz J, Fuster V. JACC State-of-the-Art Review by JACC Scientific Expert Panel. JACC. 2019 Jul 16;74(2):238-256

Development of a Multiparametric MRI Mapping Method for Pancreatic Disease. Wang L, Gaddam S, Wang N, Xie Y, Deng Z, Zhou Z, Fan Z, Jiang T, Christodoulou A, Han F, Lo S, Wachsman A, Hendifar A, Pandol S, Li D. Frontiers in Physiology. (Under review)

Cerebral Venous Thrombosis: Magnetic Resonance Black-blood Thrombus Imaging with Enhanced Blood Signal Suppression. Wang G, Yang X, Duan J, Zhang N, Maya M, Xie Y, Bi X, Ji X, Li D, Yang Q, Fan Z. Am. J. Neuroradiol. (Under review)

Coronary hyper-intensive plaques identified by coronary atherosclerosis T1weighted characterization correlate with high-risk plaque features and clinical severity in patients with acute coronary syndrome. Liu W, Wu S, Wang Z, Du Y, Fan Z, Dong L, Guo Y, Liu Y, Bi X, An J, Zhou Y, Liu W, Li D, Yu W, Xie Y. Eur Heart J Cardiovasc Imag. (Under review)

Characterization of atherosclerotic carotid plaque using MATCH: clinical validation against the conventional multi-contrast MR protocol and pathohistological analysis. Yang L, Fan Z, Du Y, Dong L, Xie Y, Wang Z, Bi X, An J, Zhang T, Laub G, Yu W, Li D. Radiology. (Under review)

Noninvasive functional evaluation of coronary stenosis using MR instantaneous wave-free ratio (MR-iFR): initial patient study. Deng Z, Lee S, Xie Y, Fan Z, Nguyen C, Bi X, Zhou Z, Shaw J, Yang Q, Choi B, Kim J, Berman D, Li D, Chang H. Radiology. (Under review)

Spotty calcium on cervicocerebral computed tomography angiography associates with increased risk of ischemic stroke. Zhang F, Yang L, Gan L, Fan Z, Zhou B, Deng Z, Dey D, Berman D, Li D, Xie Y. Stroke, 2019 Apr. doi:10.1161/STROKEAHA.118.023273

Non-invasive monitoring of allogeneic stem cells delivery with dual modality imaging-visible microcapsules in a rabbit model of peripheral arterial disease. Fu Y, Weiss C, Kedziorek D, Xie Y, Tully E, Shea S, Solaiyappan M, Ehtiati T, Gabrielson K, Wacker F, Bulte J, Kraitchman D. Stem Cells International, 2019 Mar. doi:10.1155/2019/9732319

Recent advances in cardiac magnetic resonance imaging. Lee S, Nguyen C, Xie Y, Deng Z, Zhou Z, Li D, Chang H. Korean Circ J, 2019 Feb. doi: 10.4070/kcj.2018.0246

Heart-Rate Independent 3D Myocardial BOLD MRI at 3T with Simultaneous 13N-Ammonia PET Validation. Yang HJ, Dey D, Sykes J, Butler J, Bernaski H, Kovacs M, Bi X, Sharif B, Cokic I, Tang R, Slomka PJ, Prato FS, Dharmakumar R. Radiology. 2020 Apr;295(1):82-93.

PET/MR Imaging in Myocardial Inflammation Post-Myocardial Infarction. Wilk B, Weisenberg G, Dharmakumar R, Thiessen JD, Goldhawk DE, Prato F. Hybrid. J Nucl Cardiol. 2019 Dec 3. doi: 10.1007/s12350-019-01973-9.

IEEE Trans Med Imaging Chartias A, Papanastasiou G, Wang C, Semple S, Newby D, Dharmakumar R, Tsaftaris SA. Med Image Anal. 2019 Dec;58:101535. doi: 10.1016/j.media.2019.101535. Epub 2019 Jul 18.

3D-Printed Coronary Implants are Effective for Percutanoeus Creation of Swine Model with Focal Coronary Stenosis. Colbert CM, Shao J, Hollowed JJ, Currier JW, Ajijola OA, Fishbein GA, Duarte-Vogel SM, Dharmakumar R, Hu P, Nguyen KL. J of Cardiovascular Translational Research (April 2020, in Press).

A Multi-Center Study on the Diagnostic Performance of Native-T1 CMR of Chronic Myocardial Infarctions at 3T. Circulation: Cardiovascular Imaging. Wang G, Lee S, Yang Q, Sadras V, Patel S, Yang HJ, Sharif B, Kali A, Cokic I, Tighiouart M, Collins J, Li D, Berman DS, Chang HJ, Dharmakumar R. June 2020, 13:e009894.

\*Highlighted in a 2019 review article by Harvard cardiologists on novel imaging approaches for diagnosis of ischemic heart disease in women. [ doi: 10.15212/CVIA.2019.0007 ]