New Cardiology Chair at Mayo Clinic in Arizona

Luis R. Scott, M.D., has been named the new chair of the department of cardiology at Mayo Clinic in Arizona. Dr. Scott succeeds Win-Kuang Shen, M.D., who held the position for eight years. Dr. Scott is a native of Sao Paulo, Brazil, and received his medical degree from Escola Paulista de Medicina in Sao Paulo. He completed his internal medicine residency at Albert Einstein Medical Center, his cardiology fellowship at Alton Ochsner Medical Center, and his electrophysiology fellowship at Indiana University Medical Center. He joined the Mayo Clinic staff in 2002. Dr. Scott launched the clinical cardiology electrophysiology training program at Mayo Clinic in Arizona and served as the director of the program for 10 years. His research has focused on atrial fibrillation and device therapy.

Cardiovascular Innovation Center Advances the Science

Mayo Clinic is a recognized world leader in developing innovative approaches to the science and delivery of medical care. In the last decade, there has been tremendous growth and expansion in innovative pursuits to address the unmet needs of the patient, the provider, and the health care system. To facilitate those endeavors, the Mayo Clinic department of cardiology formed the Virtual Reality Innovations Group, directed by Suraj Kapa, M.D., electrophysiologist at Mayo Clinic in Rochester, Minnesota.

Augmented and Virtual Reality

Augmented reality (AR) and virtual reality (VR) describe disruptive technologies that have the potential to vastly change the landscape of cardiology practice and approach to patient care. VR is a completely simulated, interactive, and computer-generated experience. Any type of sensory feedback can be incorporated; although most environments utilize visual and auditory feedback, medical systems frequently also incorporate tactile feedback. AR involves real-world objects and environments overlaid seamlessly with computer-generated perceptions. AR starts with the real world and alters the environment, while VR creates a totally simulated world.
Dr. Kapa and his colleagues use DICOM (Digital Imaging and Communications in Medicine) images from computed tomography or magnetic resonance imaging to create a “virtual” 3D space, providing an immersive and engaging new way to visualize patient images. This technique provides a remarkably different perspective to both planned procedures and patient care (Figure 1). In patients with complex congenital heart disease undergoing cardiac ablation or device procedures, this technology recreates patient regional anatomy in a 3D space, appreciating subtle patient anatomical variations as well as relationships to collateral structures. It has also been successfully applied to help with pre-procedural planning in patients with implanted cardiac devices undergoing extraction. In addition, VR techniques are proving to be a valuable tool in the training of residents and fellows. Future additions to this lab will include tactile and haptic feedback, which will bring realistic touch, force feedback, and precise motion tracking.

Artificial Intelligence

Artificial intelligence (AI) has the ability to detect and recognize patterns that elude humans, providing unique opportunities to further understand disease pathophysiology, diagnoses, and treatments. AI has already shown tremendous promise, with the FDA approving three AI medical devices last year. The cardiology innovation lab is fully immersing itself in AI and applying AI to the many different facets of our current practice. The use of AI to detect asymptomatic left ventricular dysfunction from the surface ECG was discussed in a prior edition of Mayo Clinic Cardiovascular Update. Dr. Kapa’s team is currently exploring the application of AI algorithms to the ECG in sinus rhythm to screen for occult atrial fibrillation (AF). They used a cohort of 77,428 Mayo Clinic patients to develop and test their AI algorithm. Using the developed algorithm, they identified an electrocardiographic signature during normal sinus rhythm that could predict with excellent accuracy an AF diagnosis [area under the curve 0.84, sensitivity 76.1%, specificity 76.4%, overall accuracy of 76.4%].

About 20% of patients with a stroke from AF were unaware of AF prior to the stroke diagnosis. Although the U.S. Preventive Services Task Force has concluded that there is insufficient evidence to determine whether the benefits of screening asymptomatic individuals for AF outweigh the harms, development of cost-effective methods to detect those patients at risk of developing AF could provide an opportunity to implement primary and secondary treatment strategies and reduce the risk of complications from AF (such as stroke).

Novel Devices and Procedures

Novel device and procedure development and testing is another focus of the Cardiology Innovation Center.

- **Minimal Invasive Pericardiectomy for Treatment of Heart Failure With Preserved Ejection Fraction**

Half of patients with heart failure have a preserved ejection fraction (HFpEF), and unfortunately to date there are very few effective treatments available. Samuel J. Asirvatham, M.D., and Barry A. Borlaug, M.D., have developed a minimally invasive pericardiectomy approach as a potential treatment option for HFpEF patients. The hypothesis is that removal of the pericardium will lead to improved effective LV diastolic compliance (even as myocardial properties remain unchanged) because the external constraining effect of the pericardium has been eliminated. Results to date are encouraging, demonstrating that percutaneous resection of the pericardium, performed in a minimally-invasive subxiphoid procedure, attenuates the rise in left ventricular filling pressures during volume loading in normal dogs and in a hypertensive pig model with features of human HFpEF (Figure 2). In addition to reduced filling pressures, improvements in left ventricular
volume with saline loading were also observed. Drs. Asirvatham and Borlaug have received a Mayo Clinic "Transform the Practice" Award for this project, and a patient pilot is planned.

- **Carbon Nanotube (CNT) Patches to Facilitate Cardiac Conduction**

Current treatment approaches for ventricular arrhythmias (VA) focus on antiarrhythmic medications or cardiac ablation to achieve tissue homogenization or to physically disrupt regions of slowly conducting myocardium. Although more patients are being treated with ablative approaches, sometimes ablation is not feasible, leaving the patient with limited alternatives. A team lead by Dr. Kapa is studying the application of a biopatch with mechanical, electrical, and physiological properties consistent with native cardiac tissue to these areas of slow conduction. To produce the biopatch, they created a nanofibrillated cellulose single-walled carbon nanotube bioink, and used it to 3D-print desired conductive patterns. The end product is a carbon nanotube biopatch that is flexible, mechanically robust, and most importantly highly conductive, allowing propagation of conduction between two different zones of normal cardiac tissue but bypassing the disrupted zone. The biopatches were tested on canines in vivo, where a thoracotomy was performed to expose the ventricular surface and an incision was made in the myocardium to create a surgical disruption. With passive application of the biopatch, restoration of the cardiac electrical wavefront activation pattern returned to baseline (presurgical incision, Figure 3). This study truly demonstrates a potential novel approach to arrhythmia therapy.

Researchers across the entire Mayo Clinic enterprise continue to explore the application of these pioneering technologies to advance the science and improve patient care.
ECG-enabled Textiles Offer Innovative Cardiac Monitoring Option

A Mayo Clinic cardiovascular team is focusing on improving patient care through a novel approach: heart monitoring via sensors embedded directly in the fibers of clothing. ECG-enabled textiles are a new form of wearable medical technology giving rise to the era of “smart heart” clothing.

Smart heart clothes hold the potential to offer 24/7 heart rhythm monitoring remotely, and to detect rhythm abnormalities early. The rapid interventions this makes possible can significantly improve the ability to detect conditions such as atrial fibrillation (AF) in order to treat patients earlier.

“Mayo Clinic collects and processes a lot of pertinent heart rhythm data, but all these generally require patients to be on site at a Mayo location to hook up the equipment,” says Peter A. Noseworthy, M.D., electrophysiologist at Mayo Clinic in Rochester, Minnesota and director of the Heart Rhythm and Physiological Monitoring Laboratory. Dr. Noseworthy is especially encouraged by the potential for remote health data transmission to improve care. “With ECG-enabled clothing, our practice won’t be restricted to patients who visit a Mayo Clinic site. We’ll send patients an ECG-enabled shirt anywhere in the world and the data will transmit back to us digitally. It could considerably increase our ability to reach patients around the world, make recommendations to those who can be treated remotely, and identify those who might benefit from traveling here for our services.”

Smart heart clothing is intended to replace the Holter monitor, a portable ECG monitoring device that hangs from the neck or belt and requires multiple adhesive electrodes be attached to the skin for several days or weeks. “It’s not a space that has had a lot of innovation,” Dr. Noseworthy says. “If you look at the Holter monitor, the technique most heart patients are familiar with today, it is basically unchanged from 20 years ago.”

For decades, Mayo Clinic has carefully curated and annotated patient biodata. The Mayo Clinic Cardiovascular Artificial Intelligence (AI) team has access to millions of data points within that database on heart rhythms, and they used that data to design and train proprietary algorithms to analyze patients’ cardiac rhythms.

Says Dr. Noseworthy: “If in the future, smart textiles allow us to be monitoring a massive number of patients — say, an order of magnitude more patients — then we need to have intelligent ways of analyzing that data for diagnosis and management, and I anticipate that AI will play a big role in that analysis.”

Current monitoring technology is limited by the following disadvantages, which ECG-enabled clothing seeks to overcome:

- Patients usually must travel to a health care center to get the device
- Leads can fall off, interrupting monitoring and diminishing data quality
- Daily activities such as showering are restricted

As smart heart clothing development proceeds and prototypes are tested, Dr. Noseworthy envisions expanding the project. He sees benefits in embedding textile sensors to detect and record other health data such as temperature, activity through step counts, and respiration rate.

Over the next year, the focus is on resolving regulatory and manufacturing issues, ensuring data privacy is protected, and refining the software. But he is confident that smart heart clothes will lead the change in the way patients receive care. They will usher in an era of more accessible heart monitoring in which patients are comfortable and confident, both in its quality and the care it makes possible. “There’s a lot of work that needs to be done to get this to being a practicing reality, but our goal is to transform and improve the way we monitor patients and manage disease,” he says.
HONORS

Rosalyn Adigun, M.D., Pharm.D., cardiology fellow at Mayo Clinic in Rochester, Minnesota, is the recipient of the Mayo Clinic 2019 Barbara Bush Distinguished Fellowship Award. This award is given to a trainee based on outstanding clinical performance, scholarly activity and humanitarianism.

Susan M. Halli Demeter, APRN, DNP, FNP-BC, provider at Mayo Clinic in Arizona, has received the Preventive Cardiovascular Nurses Association Terry Thomas Clinic Practice Award. This honor recognizes clinical excellence in the practice of cardiovascular prevention.

Allan S. Jaffe, M.D., cardiologist at Mayo Clinic in Rochester, Minnesota, has been named 2018 Reviewer of the Year by the European Heart Journal.

Steven J. Lester, M.D., cardiologist at Mayo Clinic in Arizona, has received the Richard Popp Excellence in Teaching Award from the American Society of Echocardiography. This award recognizes an outstanding teacher, nominated by students and peers, who epitomizes the ideal qualities of a teacher, mentor and role model in the field of cardiovascular ultrasound.

IN THE NEWS

Two cardiologists from Mayo Clinic in Rochester, Minnesota, received high honors at the 2019 American College of Cardiology Scientific Sessions meeting in New Orleans. Douglas L. Packer, M.D., electrophysiologist in the Division of Heart Rhythm Services, received the ACC Distinguished Scientist Award (Translational) for his major scientific contributions to the advancement of knowledge in cardiovascular disease. Samuel J. Asirvatham, M.D., also an electrophysiologist in the Division of Heart Rhythm Services, received the ACC Distinguished Teacher Award for his innovative and outstanding teaching characteristics and compassion.

Heidi M. Connolly, M.D., and Rajiv Gulati, M.D., Ph.D., cardiologists at Mayo Clinic in Rochester, Minnesota, have been selected as the 2019 Teachers of the Year by the Mayo Clinic Fellows’ Association. They were honored because of their superior commitment to education, mentoring, patient care and compassion.
Myocarditis Biomarker Predicts Disease Severity in Younger Males

Myocarditis is a potentially fatal inflammation of the myocardium that typically develops secondarily to viral infection, usually in young, seemingly healthy men. Its prevalence worldwide is estimated to be 0.5 to 4.0%, with reports of biopsy-proven myocarditis occurring in up to 16% of adult patients who have unexplained nonischemic cardiomyopathy.

As an important cause of acute and chronic heart failure, myocarditis is challenging for clinicians to diagnose and manage because it is characterized by an unpredictable and potentially life-threatening course of disease. Symptoms range from flu-like illness to dilated cardiomyopathy (DCM) and heart failure (HF). Currently, no screen or biomarker exists to help stratify the level of risk that myocarditis patients may be facing to guide clinical decision-making and treatment.

First Myocarditis Biomarker

Recently, an international research collaboration led by investigators at the Mayo Clinic in Jacksonville, Florida, published results that identified the first biomarker for myocarditis offering a measure of cardiac inflammation: the blood protein known as sera soluble ST2 (sST2) (Figure). In the largest study of its kind (n=303), results showed that compared to healthy controls, men ≤ 50 years of age with confirmed or suspected myocarditis had significantly elevated levels of sST2. This biomarker relationship did not hold for women of all ages or for men older than 50 years.

Correlations to NYHA heart failure class

To determine an association between sST2 and myocarditis severity, the study correlated patients’ New York Heart Association (NYHA) class to circulating sST2 levels in blood tests. Results showed that men ≤ 50 years old in NYHA classes III-IV heart failure expressed significantly higher sST2 levels than those in NYHA classes I-II. This association of sST2 level and NYHA class was not seen in men older than 50 or in women (Table).

Says Mayo’s lead researcher, DeLisa Fairweather, Ph.D., "The sST2 levels are biomarkers in the sense that they are a diagnostic tool helping physicians know who is at most risk for sudden death or progression to advanced disease. This knowledge is something they haven’t had before — and it now enables them to intervene with life-saving measures."

Dr. Fairweather sees three key implications of the study:

- Sera sST2 is a new biomarker that may be added to select cardiovascular workups to improve heart failure diagnosis and management
- When sST2 is used, results must be interpreted according to sex and age
- Sera sST2 expands diagnostic value beyond the natriuretic peptide family of biomarkers

Elevated sST2 is known to predict mortality from acute and chronic heart failure and is FDA-approved for evaluating select heart conditions. However, it had never before been tested in a large-scale study of patients with clinically suspected and biopsy-confirmed myocarditis. Most importantly, sST2 levels have never been evaluated in patients with myocarditis in the context of sex and age. Dr. Fairweather’s previous work with mouse models of myocarditis showed a sex skew toward males being more prone to developing certain kinds of inflammation and poor

Table. Demographics of patients included in study.

<table>
<thead>
<tr>
<th>Age</th>
<th>Total (n = 303) Mean 40 Range 18-81</th>
<th>Sexes Combined (n = 303)</th>
<th>Men (M) (n = 162) 48%</th>
<th>Women (W) (n = 141) 52%</th>
<th>p value (M vs. W)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NYHA class</td>
<td>(n = 268)</td>
<td>2.3 ±0.8 (n = 133) 49%</td>
<td>2.2 ±0.8 (n = 77) 29%</td>
<td>2.4 ±0.7 (n = 16) 6%</td>
<td>p = 0.16</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>(n = 280) 48.4 ±20.3</td>
<td>48.6 ±20.2</td>
<td>47.8 ±20.9</td>
<td>p = 0.79</td>
<td></td>
</tr>
<tr>
<td>NYHA Class I</td>
<td>(n = 268)</td>
<td>(n = 42) 16%</td>
<td>(n = 133) 44%</td>
<td>(n = 77) 29%</td>
<td>(n = 16) 6%</td>
</tr>
<tr>
<td>Class II</td>
<td>(n = 175) 65%</td>
<td>NYHA Class I-II</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Class III</td>
<td>(n = 93) 35%</td>
<td>NYHA Class III-IV</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Class IV</td>
<td>Total (n = 280)</td>
<td>LVEF &gt;45% (n = 162) 58%</td>
<td>LVEF ≤45% (n = 118) 42%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Katelyn A. Bruno, Ph.D., DeLisa Fairweather, Ph.D.
heart function. Their mouse studies also demonstrated that increased testosterone significantly raised levels of sST2, yet the female sex hormone estradiol did not. These findings suggested a role for testosterone in human myocarditis.

Says Katelyn A. Bruno, Ph.D., the study’s co-lead author, "Because of our lab’s experience in studying sex differences in disease, we looked at myocarditis by sex and age. When we divided out the results by men and women, we found that the level of sST2 in females had no relation with severity or progression of disease." The team has now developed a large international research network, including nearly 1,000 myocarditis patients and 3,000 dilated cardiomyopathy patients. The goal, Dr. Fairweather says, is to develop a more powerful suite of diagnostic tools and management approaches for myocarditis. "All this might lead us to discover more biomarkers and treatments for this disease so we can intervene before it progresses to heart failure."

For more information about the study, please see: Coronado M.J., et al. Elevated sera sST2 is associated with heart failure in men ≤50 years old with myocarditis https://www.ahajournals.org/doi/pdf/10.1161/JAHA.118.008968

**Figure. Schematic demonstrating the pathway by which intravascular levels of sST2 can increase in myocarditis.**

**HONORS**

Jae K. Oh, M.D., cardiologist at Mayo Clinic in Rochester, Minnesota, has received the Physician Lifetime Achievement Award from the American Society of Echocardiography. This honor, the society’s highest award, is in recognition of his many years of outstanding service and contributions in the field of cardiovascular ultrasound imaging, as well as the research and education he has provided at local, national and international levels.

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August 2-4, 2019  
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Rochester, MN

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August 29, 2019  
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September 6-8, 2019  
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**Cardiac Rehabilitation Workshop: The Mayo Clinic Model**  
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**Innovations in Atrial Fibrillation Management: Impacting Quality of Life and Stroke Risk**  
October 18-19, 2019  
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Scottsdale, AZ

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December 12-14, 2019  
Chicago, IL

**Echo on Marco Island: Case-Based Approach**  
December 16-19, 2019  
Marco Island, FL

**Cardiology Update at Puerto Vallarta: A Focus on Prevention**  
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Puerto Vallarta, Mexico

**Hawaii Echo With Multimodality Imaging**  
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Maui, HI

**Arrhythmias and the Heart: A Cardiovascular Update**  
January 27-31, 2020  
Kohala Coast, HI

**Cardiovascular Conference at Snowbird**  
February 5-8, 2020  
Snowbird, UT

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February 24-28, 2020  
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