Northern California Institute for Research and Education

DNA

DETAILS NEWS AWARDS

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FOCUS on Research

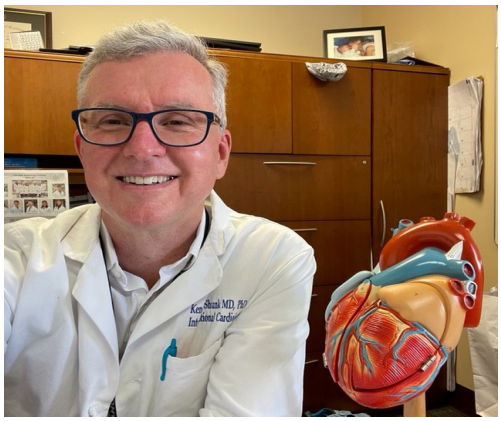
Boon in Interventional Cardiology Technologies, But Which Works Best?

When German Cardiologist Andreas Gruentzig performed the first coronary balloon angioplasty on an awake human patient in 1977, it jumpstarted the field of Interventional Cardiology and sparked a technology revolution.

The procedure – in which a tiny balloon-tipped catheter is threaded into a blocked vessel to widen it and improve blood flow to the heart – has evolved into a desirable alternative to coronary bypass surgery for some patients with clogged arteries. Traditional open heart or vessel bypass surgery typically requires several days of postsurgical hospitalization and weeks to months of recovery and rehabilitation. With angioplasty, patients are usually out of the hospital the morning after the procedure or even sometimes the same day, and are back to normal life in a few days.

In the 1980s, coronary stents were developed to improve short and long-term vessel patency from angioplasty. "Angioplasty with a stent," involves placing a small metallic spring-like device at the site of the blockage to serve as a scaffold to keep the artery open. While these technologies offered a nice repair, improved artery flow and were an alternative to invasive surgery, there were drawbacks. Some of the early stents caused complications due to their bulkiness and density; and none could guard completely against some of the physiological changes. It was not uncommon for some to suffer from calcification or scar tissue that occur in diseased arteries, angioplasty and stent-repaired or not. With the earlier generation stents, the need for repeat procedures was also not uncommon.

"We want to minimize the chance that a patient will have a return of symptoms and need to undergo a repeat angioplasty or stent procedure, or even an invasive bypass surgery following the initial decision for angioplasty," said Kendrick A. Shunk, MD, PhD, Interventional Cardiologist, UCSF Professor of Medicine, and Director of Interventional Cardiology and the Cardiac Catheterization Laboratory Research Program at the SFVAHCS.



Kendrick A. Shunk, MD, PhD,
Professor of Medicine, UCSF
Director, Interventional Cardiology, SFVAHCS
Director, Cardiac Catheterization Laboratory Research Program, SFVAHCS

More, improved technology

The last three decades have seen a boon in interventional cardiology innovations that include stents made of thinner struts of advanced alloys and biocompatible polymer coatings. These stents reliably release appropriate local doses of growth inhibitory drugs to tamp down the response to injury and prevent intimal hyperplasia, which is essentially excessive scar tissue that can reblock the lumen. These "drug-eluting stents" have become the standard of care and keep the need for re-intervention to very acceptable low levels, said Shunk.

Just in the last few years, interventional cardiology has seen dramatic developments such as the use of advanced 3-D imaging to guide the delicate procedures and transcatheter aortic valve replacement, a minimally invasive heart procedure to replace a thickened aortic valve that can't fully open.

Recent technological advances allow interventional cardiologists to treat a wider range of conditions – not just diseases such as atherosclerosis, but also more complex diseases and cardiovascular structural defects.

New technologies, however, raise new questions and challenges. Which are effective, or not? How do practitioners and patients know which technology or procedures may work best for them? Are "new" technologies actually more effective than some of the "old" or current ones?

Comparing technologies

Shunk not only has performed thousands of procedures at the SFVAHCS, he is also a national leader in the study of novel technologies and strategies to treat cardiovascular disease.

He has published numerous studies and participated in many clinical trials of interventional cardiology products and techniques, serving in essentially every role from site investigator to planning committee member to executive committee member to data safety monitoring committee member to endpoint committee member. Since 2010, he has served on the VA Cardiovascular Assessment and Reporting and Tracking (CART) Executive Committee, and for the past six years he has co-chaired the VA CART's FDA Device Surveillance Program.

His VA studies have analyzed transcatheter valve therapies and drug-eluting stents, including for diabetic patients with heart problems caused by narrow arteries, and more.

"Interventional cardiology is an exciting field that has seen some truly game-changing developments in recent years," said Shunk. "But numerous clinical questions remain and sometimes the challenge is that there are many ways to address certain situations and it is unclear which strategy is best."

"Each may have its theoretical pros and cons," he said. "We owe it to our patients to admit we don't always know the best strategy and to ask, when appropriate, for their willingness to participate in a randomized study to help sort out the answer for future patients."

"Also, our future interventionist trainees not only need to be trained and skilled in many more new techniques to treat a broader group of patients, but they also benefit from exposure to and active participation in the clinical research projects going on in the cath lab," said Shunk. "It adds an additional layer of excitement and relevance to the training experience for our fellows."

Trials compare strategies

Shunk currently is a co-investigator in two nationwide, industry co-sponsored clinical trials. One randomized clinical trial compares two treatments for patients with severely calcified lesions, or blockage: Orbital atherectomy, which uses a diamond-coated crown that spins back and forth inside the blocked vessel to sand and reduce the calcium, versus conventional angioplasty followed by drug-eluting stents.

The study – called ECLIPSE and sponsored by Cardiovascular Systems, Inc., which developed the orbital device – will eventually enroll into the trial some 2,000 patients at 80 centers in the United States. Half of the participants will receive the orbital atherectomy before drug-eluting stent implantation, while the other half will receive the conventional angioplasty and drug-eluting stents. It's the largest randomized trial to date specifically designed to assess the strategy of adjunctive coronary atherectomy for calcific coronary artery disease.

At the SFVAHCS, 41 patients have undergone one of the two procedures to fix their blocked vessels. Each will be followed long-term to assess the two different strategies.

In another study, Shunk is among investigators in the first United States (US) clinical trial to evaluate the safety and effectiveness of a novel drug-coated balloon for patients with coronary stent restenosis (when a stent-treated vessel becomes blocked again). The blockage, which may happen within six months after the first stent procedure, occurs because new tissue grows inside the stent and obstructs blood flow.

The study – called "AGENT Investigational Device Exemption" and sponsored by Boston Scientific – evaluates a percutaneous transluminal angioplasty balloon that is coated with a drug targeted to the restenosis. The balloon opens narrowed vessels and then delivers the drug to the vessel wall without necessarily a need for additional layers of stent.

The study is comparing the technology to "plain old balloon angioplasty." At 40 US sites, 480 patients will receive one of the two procedures and will be followed for health outcomes after at least a year. The SFVAHCS is the only VA Medical Center in the study.

Like other scientists at the SFVAHCS, Shunk has an affinity and appreciation for Veterans, who are often willing and cooperative research participants.

"They are an incredibly altruistic group," said Shunk. "Sometimes, their research participation won't necessarily help them individually. But they are part of important data to evaluate possibly promising therapies."

"They tell us, if it will help someone else in the future, they are all in."

Now, that's having a big heart. ♥

Q and A: An Interview with Dr. Arthur Wallace

Arthur Wallace, MD, PhD
Chief of Anesthesia Service, SFVAHCS
Professor and Vice Chair of Anesthesiology and Perioperative Care, UCSF

Q: Your longtime research has focused on reducing health risks and complications in cardiac surgery patients. What are some highlights of your research?

A: We initially conducted epidemiologic analysis to understand the risk factors for perioperative cardiac morbidity and mortality, then did prospective, randomized controlled clinical trials of medications that would reduce the risk factors we identified and found two medications that reduced the risk of death. We started using those medications in our anesthesia preop clinic, and our observed-to-expected mortality rate was reduced from 1.0 to 0.6, a 40 percent reduction in mortality.

We then assisted many hospitals to implement protocols and reduced perioperative mortality rates by 35 percent. We conducted epidemiologic analysis to identify new medications for cardiac risk reduction and found that rather than needing to develop a new medication, the most important factor was medication compliance. We then focused on methods to improve medication compliance with anti-ischemic agents. We published one of the very few papers where the entire process of developing and then implementing a Level 1 standard of care was shown to be associated with a reduction in mortality.

Q: Your research has shifted toward COVID-19. Tell us how your cardiac care research is being applied.

A: When the COVID pandemic began, I realized that the algorithms we had developed to identify medications to reduce perioperative cardiac morbidity and mortality would be equally effective in identifying medications to reduce COVID-19 morbidity and mortality. We used the Veterans Affairs' Corporate Data Warehouse (CDW) to identify therapies for COVID-19.

We identified four classes of medications associated with a reduction in mortality from COVID-19. We then recognized the significant problem of long-term sequelae of COVID-19 infection and have been working to fund research to identify medications to reduce the incidence, severity, and duration of post-acute sequelae of COVID-19 infection. At present, there are no known therapies for long COVID. We hope our work in identification of medications associated with a reduction in COVID mortality will ultimately identify therapies for long COVID.

Q: How and why is the VA well-suited to conduct these COVID-related studies?

A: When the COVID pandemic began, I recognized the problem and started trying to obtain data from China. We translated our requests into Chinese and searched out data but were unable to gain access. When the pandemic struck Italy, we translated our requests into Italian and were more successful with finding a data source, but the restrictions on access seemed prohibitive.

By that time sufficient cases had accumulated in the United States, there were enough cases in the VA CDW to have sufficient power to do analysis. The VA CDW is updated every 24 hours and the data is nationwide, representing about 4 percent of the U.S. In our last study (Nov. 4, 2021), there were 800,000 patients who had been tested with more than 265,000 COVID cases. This database represents more cases than 165 other countries, is nationwide, and is updated daily. The CDW curates the data making analysis faster and more accurate. It is a national treasure that is essential for public health surveillance and research.

Q: Researchers at the SFVAHCS were quick to rally around the COVID emergency to adapt their research and use their expertise to fill some urgent needs. Give an example.

A: Many people at the SFVAHCS collaborated to respond to the pandemic. It would be most appropriate for me to only comment on the efforts of the Anesthesia Service. Staff in the Anesthesia Service wrote protocols for care of patients, developed protocols for PPE use in the OR, served on committees for testing PPE etc., worked to acquire the best equipment and supplies possible, used 3D printing and other approaches to manufacture hard-to-get equipment, set up an operating room to handle COVID-infected patients who are extremely high risk to staff and for adverse outcomes, repurposed ventilators, worked on therapies for COVID, trained staff on COVID protocol, and provided the best clinical care possible to patients throughout the pandemic. The SFVAHCS staff did an exceptional job over a prolonged pandemic providing the best care possible.

Q: What is the next step for your research?

A: COVID-19 infection is a multi-system disease affecting the microvasculature, respiratory, cardiac, renal, autonomic, and nervous systems. Some fraction of patients (10-80 percent, depending on the study) who get COVID-19 have long term sequalae of COVID-19, including

An Interview with Dr. Arthur Wallace Continued

shortness of breath, exercise intolerance, confusion, anxiety, depression, autonomic dysfunction, cardiac, and renal problems. Fifty percent of patients have symptoms a year after COVID infection.

We are working to identify medications to reduce the incidence, duration, and severity of the post-acute sequelae of COVID-19, also known as long COVID or COVID Long Hauler Syndrome. There was a question of the effects of vaccination on long COVID, which led us to look at vaccine efficacy. The effects of vaccination and boosters on long COVID will be included in this work.

Q: What would most people be surprised to know about you?

A: I work on a number of projects in addition to this work on medication development. I really enjoy inventing medical devices and therapies. I developed the endotracheal cardiac output monitor (ECOM), and I am now working on a remote, non-contact, patient monitor (Audiovisual Detection Monitor) that uses machine vision to measure heart rate, respiratory rate, pulse oximetry, perfusion, pain, delirium, obstructive breathing, vomiting, aspiration, out of bed alarms, and blood pressure without any sensors on the patient. It will help us simply and inexpensively monitor every patient in the hospital, and to provide the best care possible.

In the Helix

Shannon Ellis
NCIRE Purchasing Manager

Q: What are you reading currently?
A: I am currently reading A Wild Sheep Chase by Murakami Haruki

Q: When you're not working, how do you like to spend your time?
A: In my spare time I like creating art, spending time with my family and traveling when we are able.

Q: If you could instantly become an expert in something, what would it be?
A: If I could instantly become an expert in something it would probably be 3D printer technology and software!

Norina Tang, PhD
NCIRE Research Specialist

Q: What are you watching currently?
A: I am currently binge-watching the TV series called Yellowstone. What grabs me about this show are the many parallels to the conflict that exists in the United States as a whole.

Q: When you're not working, how do you like to spend your time?
A: In my spare time, I like to spend time with family and friends. I typically go hiking with my girlfriend(s), eat out and watch TV/movies with my husband, and travel. I also like to try out new recipes and cuisines.

Q: If you could instantly become an expert in something, what would it be?
A: I would love to be a good dancer. It is something I have ZERO talent for. I think it would be spectacular if I can utilize my body to the extent I utilize my brain, not to mention how great I would look in the process (hee hee)!

Tristan Moss-Vazquez
NCIRE Staff Research Associate I

Q: What are you reading currently?
A: I am currently reading The Translator by John Crowley. I've really enjoyed his other novels that fall under the Aegypt Tetralogy.

Q: When you're not working, how do you like to spend your time?
A: When I am not working, I like to spend my time either reading a book or being outdoors playing soccer, biking, or camping.

Q: If you could instantly become an expert in something, what would it be?
A: If I could instantly become an expert in something it would probably be the identification of trees. Trees are all around us and learning more about them allows me to feel more connected and appreciative of the environment.

Department Updates

DEI Advisory Group Looking for New Members

NCIRE's Diversity, Equity, and Inclusion (DEI) Advisory Group is tasked with helping NCIRE carry out its commitment to create a representative, equitable, and inclusive workplace through education and communication, with the goal of fostering mutual tolerance and cultivating respect for all people regardless of race, ethnicity, culture, physical appearance, ability, age, gender, gender identity, sexual orientation, political view, and religion.

DEI is comprised of NCIRE employees, staff, and leadership. Working together we strive to create an environment that fosters diversity and ensures equity and creates a culture of inclusion across the organization.

If you would like to join us, please contact DEI@ncire.org.

Contracts & Grants News

Effective January 2, 2022, the salary limitation for Executive Level II (also known as the NIH Salary Cap) increased to $203,700. And for NIH applications due on/after January 25, 2022, NIH requires the use of Forms-G grant application forms. As part of the Forms-G rollout, all listed Key Personnel are required to have an eRA Commons ID; and the most current Biosketch template (noted in the header with approval through 9/30/2024) and new Other Support (OS) pages must be used. Notable differences for the Biosketch includes the removal of Section D Research Support. Changes to the OS includes reorganization of how information is presented, disclosure of all resources, the inclusion of in-kind contributions, and a requirement for a verified PDF signature (not an image of a signature).

Please click the following links for detailed information regarding:

- Biosketch: https://grants.nih.gov/grants/forms/biosketch.htm
- Other Support: https://grants.nih.gov/grants/forms/othersupport.htm

Compliance Reminders:

Timesheets

In accordance with 2 CFR 200 the Uniform Guidance: Uniform Administrative Requirements, Cost Principles, and Audit Requirements for Federal Awards (Uniform Guidance), NCIRE is required to have adequate internal controls to mitigate the risk of fraud. Employee certification, along with supervisorial approval, is an essential and critical element of basic internal controls to ensure proper time and effort reporting. Employees submit bi-weekly timesheets, these are due on alternating Friday's. Please ensure timesheets are approved. Unsigned timesheets pose a compliance issue. If you are having trouble or have questions, please contact Joyce Jia, Sr. Payroll Administrator at payroll@ncire.org.

Quarterly Certifications of Sponsored Project Expenditures

NCIRE has strengthened its internal controls for direct and indirect charges to NCIRE's projects and other research support accounts. The purpose of this internal control is to document compliance with OMB Uniform Guidance. To ensure compliance NCIRE's PIs, are required to quarterly certify attesting to the accuracy of the Project Account Statements. The policy can be found here.

Grant Funding Opportunities

Industry Opportunities (as of 3/18/22)

Please contact Newton Ong newton.ong@ncire.org or at x23892 for further information on the following Industry Opportunities.

PPD
A Phase 2 Multicenter, Open-Label, Single-Arm Study to Evaluate the Safety and Efficacy of Oral XXX in Combination with Paclitaxel in Patients with Recurrent and/or Metastatic Head and Neck Squamous Cell Carcinoma, Who Progressed on or After Immune Checkpoint Inhibitor Therapy.

Aids Malignancy Consortium (AMC) (Emmes)
This study will evaluate the efficacy of the oral drug pomalidomide for treatment of KS in people living with HIV (PLWH) and HIV- persons. In May 2019, the FDA granted accelerated approval for pomalidomide in the treatment of KS based on promising results from the Phase 1/2 Polizzotto study (N = 22), showing treatment was well-tolerated and response reported in 73% of participants. The current study seeks to confirm these results in a multi-institutional setting and to provide evidence of clinical benefit as measured by 1-year response duration.

Adaptive Phage Therapeutics, Inc (Emmes)
A Phase IIa Randomized, Parallel Group, Double-Blind, Placebo-Controlled, Repeat-dose, Multi-Site Study Investigating the Safety, Tolerability, and Efficacy of Personalized Phage Treatment and Standard of Care Antimicrobials for Patients with Diabetic Foot Osteomyelitis due to S. aureus.

Effector Therapeutics
A Randomized, Double-Blind, Placebo-Controlled Trial of Tomivosertib in Combination With Anti-PD-(L)1 Therapy in Subjects With Non-Small Cell Lung Cancer as First Line Therapy or When Progressing on Single-Agent First-Line Anti PD (L)1 Therapy.

Please visit this link for the full list of Industry Opportunities.

NCIRE Federal Funding Opportunities (as of 3/17/22)

NIH funding opportunities specific to COVID-19 Research:
https://grants.nih.gov/grants/guide/COVID-Related.cfm

CDMRP: FY22 Amyotrophic Lateral Sclerosis Research Program (ALSRP) is currently accepting applications for various mechanisms. https://cdmrp.army.mil/funding/alsrp

- Pre-Application: Due Dates April 29, 2022
- Full Application: Due Dates July 28, 2022 (some by invitation only)

CDMRP: FY22 Breast Cancer Research Program (BCRP) is currently accepting applications for various mechanisms.
https://cdmrp.army.mil/funding/bcrp

- Pre-Application: Various Due Dates April 28 - May 3, 2022
- Full Application: Various Due Dates May 17 – July 27, 2022 (some by invitation only)

Please visit this link for the full list of Federal Funding Opportunities.

Congratulations to our PIs for their recent awards!

Daniel Mathalon, PhD honored with Lifetime Achievement Award

NCIRE-supported Investigator Daniel Mathalon, PhD was one of five psychological and brain sciences alumni honored by the University of Indiana at its Department of Psychological and Brain Sciences' 2021 Alumni Recognition Day back in October 2021.

Dr. Mathalon received the department's Lifetime Achievement Award for his prestigious work in the field of psychiatry.

The department, in the IU Bloomington College of Arts and Sciences, has acknowledged outstanding graduates of its bachelor's and Ph.D. programs with a series of awards since 2013, the year of the department's 125th anniversary.

Dr. Mathalon is the Deputy Vice Chair for Research at the San Francisco VA Health Care System, and professor with the Department of Psychiatry and Behavioral Sciences, Weill Institute for Neurosciences at University of California, San Francisco.

Learn more: https://today.iu.edu/live/news/704-5-psychological-and-brain-sciences-alumni-honored

Thomas Neylan, MD, 2021 Robert S. Laufer Memorial Award recipient

The International Society for Traumatic Stress Studies honored NCIRE-supported Investigator Thomas Neylan, MD with its 2021 Robert S. Laufer Memorial Award.

This award is given to an individual or group who has made an outstanding contribution to research in the field of traumatic stress. Robert S. Laufer, PhD, was a sociologist who made early and important contributions to the field of traumatic stress and PTSD through his research on the effects of war experiences on Vietnam combat veterans. Laufer was Professor of Sociology at Brooklyn College of the City University of New York and an author of the groundbreaking study of returning veterans, entitled Legacies of Vietnam: Comparative Adjustment of Veterans and Their Peers, published in 1981, with Arthur Egendorf, Ellen Frey-Wouters, and others.

Laufer and colleagues expanded the concept of combat exposure to include multiple dimensions. In particular, he focused on witnessing or participating in abusive violence, an important new focus for a guerilla war where there were no front lines, and where enemy combatants and civilians were often difficult to distinguish. He found that abusive violence followed from more extreme exposure to combat, and was associated with distinctive psychological and behavioral outcomes, including different aspects of PTSD. Laufer died prematurely of cancer in 1989 at the age of 47. This award is made in his memory.

Learn more: https://istss.org/membership/awards-and-honors

Message from the Chief Executive Officer

We are very proud to bring you the first issue newsletter for 2022. It is amazing how quickly 2022 is moving, we are in mid-March already! Given the past two years, I hope you find time to enjoy some sunshine and fresh air.

In the Fall of 2021, NCIRE became a member of the NAVREF Industry Consortium. The goal of the consortium is to bring together bio-medical research industry stakeholders with VA-affiliated Nonprofit Corporations (NPCs) to establish a regular forum for exchanging information, sharing goals, and building relationships that will generate improved collaborations and drive solutions that meet the health needs of Veterans. Currently, there are thirteen Pharma companies involved in the Consortium. The VA has posted Research Strategic Priorities for 2022. The first goal is to Increase Veterans' access to high-quality clinical trials. NCIRE will continue to communicate new clinical trial opportunities weekly.

In March there was an update to the (394) Residual Account Policy. The revised policy can be found here.

NCIRE recently concluded the FY2021 financial audit, the report will be presented to the Audit Committee. The auditors issued a clean and "unmodified" report, demonstrating there are no financial issues and that NCIRE's accounting and financial management practices meet and exceed all standards. The outcome of the audit is a result of the professionalism and dedication of the Core Administrative Staff as they work to support the Research Community at SFVAHCS.

At the end of March, Ms. Bonnie Graham, Medical Center Director will retire. We thank Ms. Graham for her support of NCIRE and research. We will miss her.

Thank you for your support of the NCIRE 2022 Spring edition with remarkable contributions from Drs. Kendrick Shunk and Arthur Wallace. Their willingness to share their research and provide their time is appreciated. Also, three NCIRE staff members have shared delightful personal details In the Helix.

NCIRE is always proud to share and promote the achievements of our Research Community. We encourage PIs and their labs to contact NCIRE Executive Assistant Tai Arceneaux at Tainese.Arceneaux@ncire.org with website links, stories, etc. about your research so that we may celebrate your work with our readers.

Rebecca Rosales, MBA, CRA
Chief Executive Officer

About NCIRE

NCIRE - The Northern California Institute for Research and Education has one mission and one goal: Advancing Veterans Health. We sustain a scientific community of clinicians and researchers and support over 200 researchers who have joint faculty appointments at the University of California, San Francisco (UCSF) and the San Francisco VA Health Care System (SFVAHCS) and are working to foster innovation through leadership in the field of Veterans health research. Our broad portfolio of projects receives generous support from the National Institutes of Health, the Department of Defense, and individual donors, making us the largest nonprofit research institute devoted to Veterans health in the US.

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