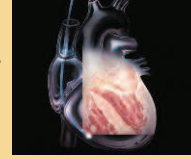




Focus Topic: Cardiovascular Imaging



Over the course of the past 20 years, several new cardiovascular imaging modalities have been developed and introduced into clinical procedures.

A quarterly publication of Queen's Heart

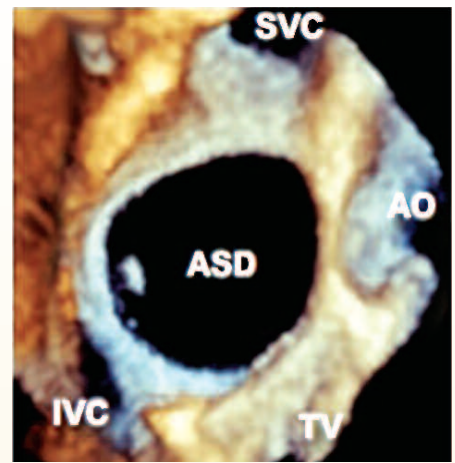
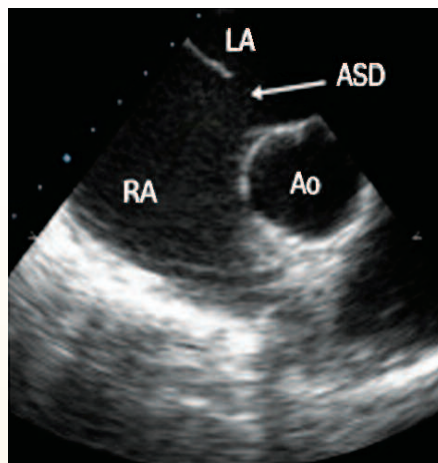
HEARTbeat

REAL-TIME 3D TRANSESOPHAGEAL ECHOCARDIOGRAPHY

Echocardiography has evolved significantly over the last half century. Developed in the 1950s, the technology has become routine in cardiologists' offices and hospitals.

Echocardiographic images are obtained largely by transthoracic imaging, where the ultrasound transducer is positioned on the patient's chest wall. Aside from M-mode imaging and Doppler technology, two-dimensional echocardiography is the standard, allowing visualization of the anatomy in one two-dimensional plane. In a certain subset of patients, transesophageal echocardiography (TEE) is needed in order to gather greater details of intracardiac anatomy. This technology became widely available in the 1980s. Similar to standard transthoracic echocardiography (TTE), two-dimensional images are obtained. During TEE, an echocardiography probe about the size of an endoscope is inserted into the esophagus and stomach, which are anatomically located just behind the heart, allowing for an unobstructed view.

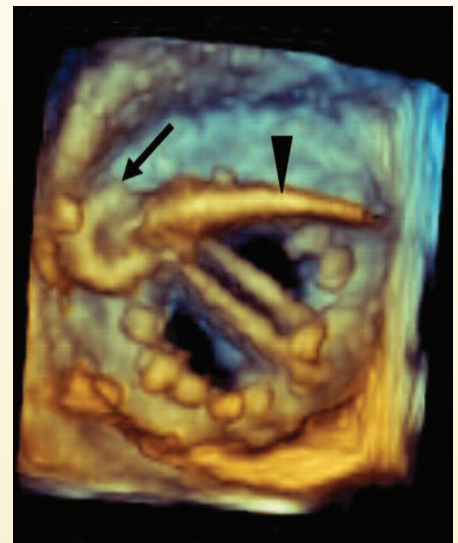
Despite this, complex intracardiac structures, such as the mitral valve or the relationship of two structures to each other, remain difficult to visualize because of the two-dimensional nature of echocardiography. The 21st century then saw the development of three-dimensional TEE (3D-TEE), which initially required post-processing of two-dimensional images. The disadvantage of this technique was that pictures were obtained and the three-dimensional reconstruction occurred after the fact, which resulted in limited use of 3D-TEE to guide procedures. More recently,



2D TEE (left) and 3D-TEE (right) of atrial septal defect (ASD). (LA: left atrium, RA: right atrium, Ao: aorta, SVC and IVC: superior and inferior vena cava, TV: tricuspid valve)

the technology has evolved to real-time 3D-TEE, meaning images are generated at the time of image acquisition.

Queen's Heart has recently acquired a real-time 3-D TEE machine. "This new piece of equipment will not only improve patient care by allowing better evaluation of anatomy prior to planned valve surgery," according to Dr. Todd Seto, Cardiologist and Director of Cardiac Non-Invasive Services at Queen's Heart, "it will also be of great utility in monitoring intraoperative results—for example, mitral valve repair surgery." Just as TEE has overcome some limitations of TTE, real time 3D-TEE has overcome some of the limitations of TEE. Dr. Chari Hart, Non-Invasive Cardiologist, comments: "Real-time 3D-TEE is also of great value for guidance of complex transcatheter procedures in the cardiac catheterization laboratory, such as paravalvular leak closures or in the evaluation of atrial septal defects prior to percutaneous closure."

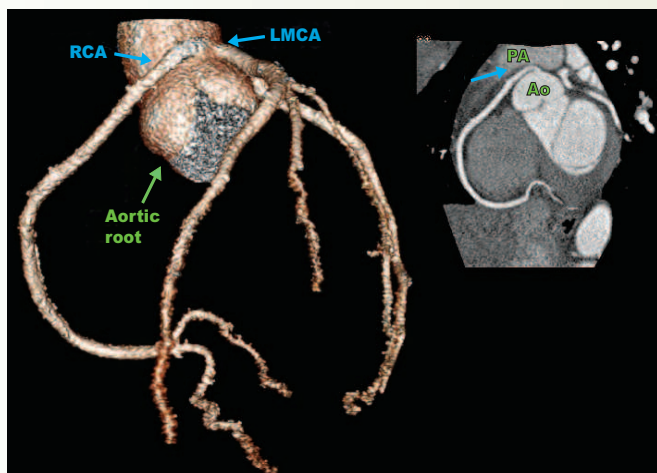


3D-TEE guidance of percutaneous paravalvular leak closure. Left atrial view of a mechanical mitral valve. The plug (arrow) used to close the leak is still attached to the delivery cable (arrow head)

CARDIAC MAGNETIC RESONANCE IMAGING AND COMPUTED TOMOGRAPHY

Over the past several years, advances in technology have allowed magnetic resonance imaging (MRI) and computed tomography (CT) scanners to acquire images of the heart.

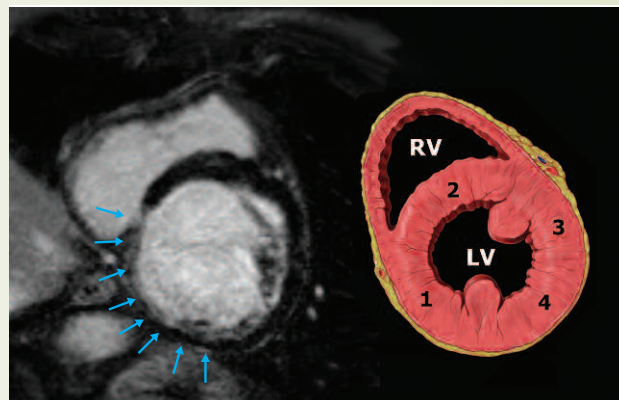
MRI has been in clinical use for decades, producing exquisite images of stationary anatomy, such as the brain, spine, and joints. However, recent advances in technology have allowed images to be acquired rapidly during suspended respiration, synchronized with an electrocardiogram (ECG) trace. Pictures of the beating heart can be obtained in any plane. If these movies are obtained in a stack of the entire heart, then special software can be used to measure the volume and function of the cardiac chambers.



Coronary CT Angiogram of an anomalous right coronary artery (RCA), taking off the left coronary cusp. On the left, a volume rendered image of the RCA and left main coronary artery (LMCA) is seen. On the right, a multiplanar reformatted image outlines the course of the anomalous coronary artery in-between the pulmonary artery (PA) and the Aorta (Ao).

Different techniques can also be used to measure blood flow and velocity, analogous to Doppler ultrasound, allowing for the evaluation of valvular disease. Further, scientists have discovered that taking images of the heart about 10 - 15 minutes after the injection of gadolinium contrast produces images with detailed visualization of areas of prior myocardial infarction. These post-contrast MRI images provide information as to which tissues in the heart are alive or dead. Although this data can be provided by a PET scan, MRI is able to provide higher resolution pictures that can show whether the layer of infarcted tissue is greater than 50% of the wall thickness of the heart muscle. “Cardiac MRI is a powerful tool, complementary to both cardiac catheterization and echocardiography,” states Dr. Darren Lum, Radiologist at The Queen’s Medical Center. “With the high spatial resolution of post contrast MRI, we are able to classify whether the heart muscle is viable or not. This can be critical information for the cardiothoracic surgeon or cardiologist contemplating whether or not to revascularize a patient who is post myocardial infarction.”

The recent explosion in CT scanner technology has allowed CT Angiography of the coronary arteries to become practical. In this test, X-rays are used to take CT images of the heart synchronized with the ECG trace. To see the coronary arteries, iodine contrast is injected into a vein and pictures are taken during diastole. In order to minimize the motion of the coronary arteries, these studies typically require the slowing down of the patient’s heart rate to 65 bpm using beta-blockers. One of the drawbacks of this test is that X-rays are used, which can be a concern for patients, given the recent uproar over the radiation dose associated with CT scans. However, advanced ECG gating techniques allow the pictures to be timed such that the X-rays are only turned on during diastole (prospective ECG gating), allowing the total radiation exposure to the patient from this exam to be reduced drastically. “With a properly performed CTA, using heart rate control and radiation dose reduction strategies such as prospective gating or retrospective ECG dose modulation, the radiation exposure associated with this exam can be reduced to below that of a routine CT of the abdomen or chest,” states Dr. Lum. The accuracy of coronary CTA has been evaluated in many scientific studies. However, the clinical utility and the role of this test in the care of the cardiac patient is yet to be determined. Conclusions from early studies suggest that the high negative predictive value of coronary CTA may be useful for low risk patients presenting with chest pain. A negative coronary CTA can be very helpful in excluding significant coronary artery disease. However, the resolution of coronary CTA is lower than that of cardiac catheterization, with degraded image quality in sections of calcified atherosclerotic plaque. In patients with acute chest pain with known coronary disease, a positive ECG, or elevated cardiac serum biomarkers, catheter-based coronary angiography should be the test of choice. On the contrary, CTA can play a valuable role in mapping the course of coronary arteries with congenital anomalous origins.



Late enhancement cardiac MRI image revealing prior myocardial infarction without significant viability in the inferior wall and its adjacent territories (blue arrows). On the right, corresponding schematic of the short axis view is shown. (RV: left ventricle, LV: left ventricle, 1: inferior wall, 2: septal wall, 3: anterior wall, 4: lateral wall).

IVUS & ICE:

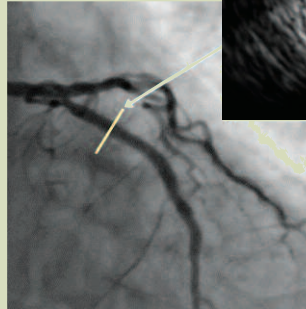
CATHETER-BASED ULTRASONOGRAPHY IN THE CARDIAC CATHETERIZATION LABORATORY

Traditionally, the imaging modality of choice in the cardiac catheterization laboratory is x-ray. However, over the course of the last 20 years, additional imaging techniques have been added to overcome certain limitations of conventional coronary angiography.

Several of these techniques are ultrasound-based. Aside from use of transthoracic (TTE) or transesophageal echocardiography (TEE) guidance for procedures, such as pericardiocentesis or complex structural procedures, certain ultrasound imaging techniques are catheter-based. By positioning ultrasound-capable catheters inside cardiac structures, one can obtain additional valuable information, which otherwise would be hidden from the conventional angiographers eyes. Among these catheter-based ultrasound techniques are intravascular ultrasound (IVUS) and intracardiac echocardiography (ICE). Both imaging technologies are being routinely used to guide coronary and structural interventions in the cardiac catheterization laboratory.

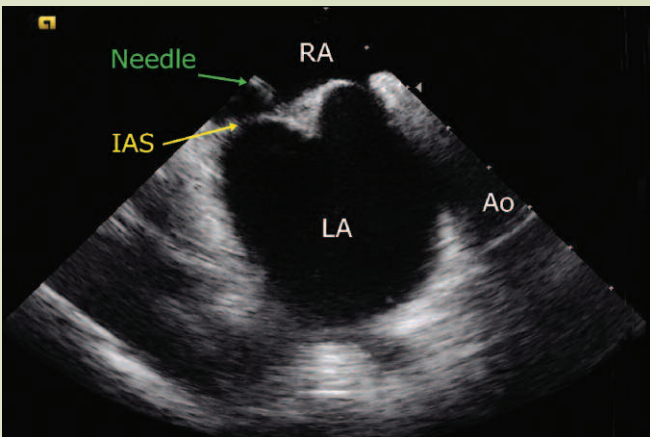
IVUS is a technique used to evaluate coronary arteries. It is a catheter of only about 1 mm in diameter. A miniature ultrasound probe at the tip of the catheter provides an inside look of the coronary artery in a 360 degree surround view. Dr. John Cogan, Interventional Cardiologist, points out, “The technique not only allows more accurate evaluation of the extent of coronary artery disease—it actually visualizes the atherosclerotic plaque directly.” IVUS is frequently used to evaluate so called intermediate lesions—especially the left main coronary artery—to help decide whether revascularization would be indicated. Dr. Christian Spies, Interventional Cardiologist adds: “It also helps guiding interventional procedures, such as stent placement, as it much more accurately determines correct stent placement.”

Intravascular ultrasound (IVUS) and angiogram of a coronary artery after stent placement. On the angiogram, the stent (not visible itself) appears well expanded, as the size of the stented artery is identical to the adjacent arterial segments (below).

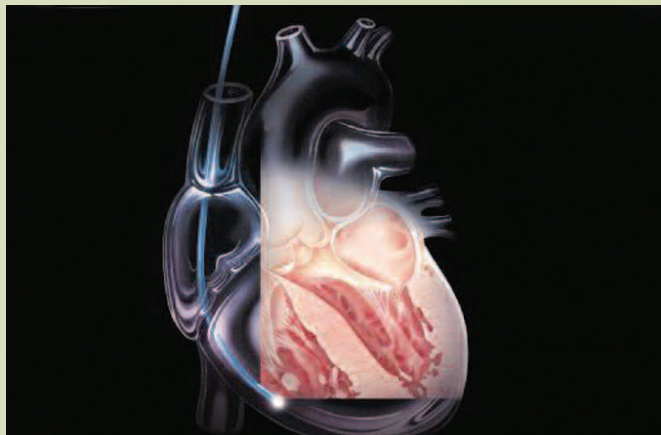


On the transverse IVUS image, the stent is clearly smaller than the artery, consistent with inadequate stent expansion. This may lead to future problems, such as restenosis. (blue: IVUS catheter, red circle: outline of stent, red arrow: stent strut, green circle: inner lumen of the artery.)

On the other hand, ICE provides images which are comparable to two-dimensional echocardiograms such as TTE or TEE. The difference, however, is that the echo probe with ICE is advanced via the femoral vein into the right atrium. This allows superb imaging, especially of atrial structures. It is used to guide structural interventional procedures in the cardiac catheterization laboratory. The main utility is in guidance of percutaneous patent foramen ovale or atrial septal defect closure. By using ICE as opposed to TEE in the guidance of these procedures, patients do not require general anesthesia, which is usually needed if a TEE probe is left in place to guide a procedure. Another area where ICE is beneficial is in gaining access to the left atrium via trans-septal puncture. “Trans-septal puncture traditionally has a 2% rate of major complications. With ICE, the needle used to puncture the inter-atrial septum can be visualized directly, allowing a much safer and controlled procedure,” according to Dr. Christian Spies, who introduced ICE at Queen’s Heart.



Intracardiac echocardiography for guidance of transseptal puncture. The needle, advanced via the inferior vena cava is clearly visualized as it is tenting the inter-atrial septum, avoiding mispuncture into the right atrial free wall or the aorta (IAS: inter-atrial septum, RA: right atrium, LA: left atrium, Ao: aorta)



Intracardiac echocardiography – A less than 3 mm in diameter measuring probe is inserted into the right heart chambers, providing detailed images of the heart.

STRESS TESTING LABORATORY

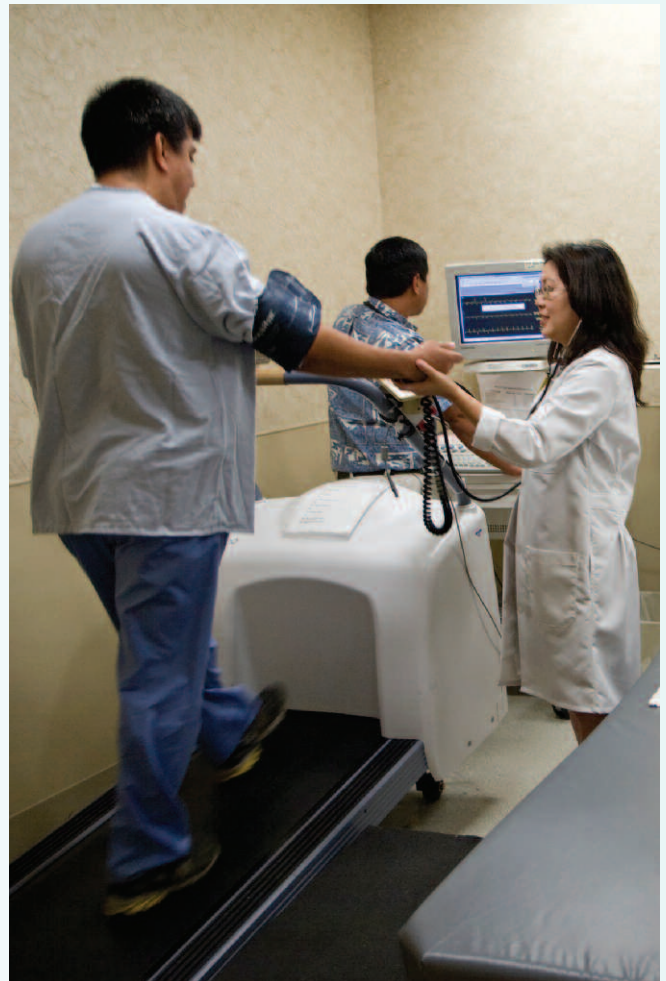
The Centers for Disease Control and Prevention reported that 631,636 people in the United States died of heart disease in 2006. Heart disease accounted for 26% of all deaths that year, with the vast majority of those resulting from coronary artery disease (CAD).

Clearly, the U.S., including Hawai'i, faces an enormous CAD burden, and appropriate diagnosis and treatment is essential for health care professionals. Cardiac stress testing is an integral component of CAD evaluation. American College of Cardiology (ACC) and American Heart Association (AHA) guidelines state that indications for stress testing include:

- Patients undergoing initial evaluation with suspected or known CAD.
- Patients with suspected or known CAD previously evaluated and now presenting with significant change in clinical status.
- Certain patients after acute coronary syndrome for risk stratification purposes.
- Perioperative cardiac evaluation for non-cardiac surgery in a certain subset of patients.

The Queen's Heart Non-Invasive Laboratory offers a full array of services, including non-invasive diagnostic testing and all types of echocardiography. In 2009, Queen's Heart performed over 3,000 stress tests, of which 1,300 were exercise stress echocardiograms and another approximately 1,300 exercise electrocardiogram (ECG) stress tests and 274 pharmacologic stress echocardiograms. These large numbers are complemented by another 750 exercise nuclear stress tests done in collaboration with the Nuclear Medicine Division. Finally, another 1,200 pharmacologic stress myocardial perfusion scans were done in Nuclear Medicine directly.

It is important to determine which stress test to order. "Exercise stress has many advantages over pharmacologic stress, as it is not only the most physiologic, but also provides important data on cardiovascular function, hemodynamic response, and exercise capacity," points out Dr. Chari Hart, Non-Invasive Cardiologist at Queen's Heart. Exercise capacity in of itself in some studies was the strongest predictor of mortality and cardiovascular events. However, if the patient is unable to exercise, then pharmacologic stress needs to be considered. Patients at Queen's Heart will have a baseline ECG and vital signs checked and then screened by a cardiologist for the appropriateness of the test ordered. The cardiologist can then discuss with the referring physician if any changes should be made on the choice of test.



Exercise Stress Echocardiogram. First, the patient is exercised on a treadmill.



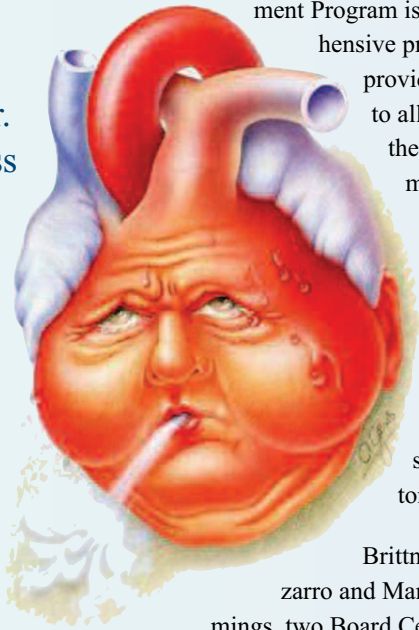
Exercise Stress Echocardiogram. Immediately following exercise, echocardiographic pictures are taken.

QUEEN'S HEART FAILURE DISEASE MANAGEMENT PROGRAM

In the United States, there are nearly five million people living with heart failure (HF), and approximately 600,000 new patients are diagnosed every year. HF-related illness is growing at an astounding rate each year.

Of diagnosed patients, many of them will not receive the appropriate treatment or the continued follow up that is needed to reduce morbidity and mortality. Numerous studies have documented the under-utilization of evidenced-based treatment options, such as the use of ACE inhibitors and beta-blockers. The recent development and trend of heart failure disease management programs have shown a reduction in mortality, as well as hospital readmissions. Current guidelines include recommendations for disease management programs for high risk patients with HF.

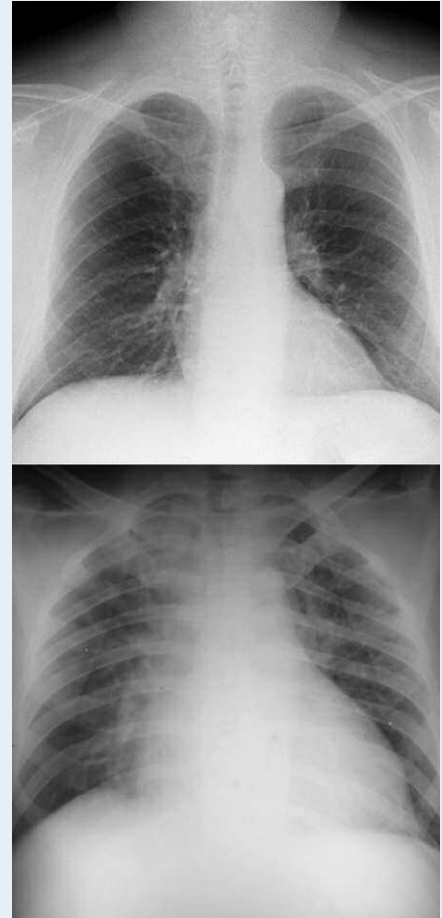
The American College of Cardiology (ACC) and the Institute of Healthcare Improvement (IHI) have recently set a goal to reduce HF-related admissions in the United States by 20% before the year 2012. This Hospital to Home Initiative (H2H) was created to enroll hospitals to collaborate in an effort to achieve this goal. The Queen's Medical Center has joined this program and committed re-



sources to do its part. The H2H initiative focuses on three main goals: medication management, early follow up, and symptom management. The goal at the Queen's Heart Failure Disease Management Program is to create a comprehensive program that strives to provide high quality care to all HF patients with these three goals in mind. Initiatives include inpatient support and education, dietary consultation, medication education by a team of pharmacists, outpatient follow up services, and symptom management.

Brittney Patterson-Lazarro and Mandi Benton Cummings, two Board Certified Nurse Practitioners (NP), provide direct care and coordinate heart failure treatment with the patient and primary health care provider. The program is overseen by Drs. Christian Spies and Robert Hong, cardiologists at Queen's Heart Physician Practice. The Disease Management Program provides patients with an opportunity to optimize medications recommended for heart failure patients based on national treatment guidelines; frequent assessments of patients; improvement of quality of life by providing education; and ultimately, decreasing the need for hospitalization and emergency department visits.

Once enrolled in the program, the NPs assist patients with lifestyle changes by providing a better understanding of their conditions so that they can manage and



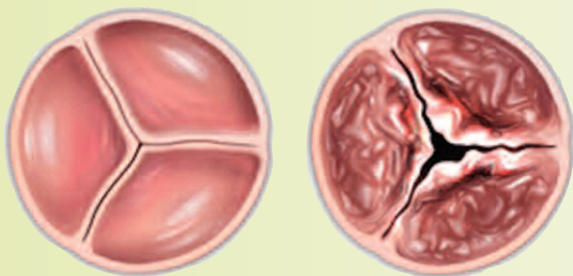
Normal chest X-ray (top) and chest X-ray of a patient with acute decompensated left heart failure (bottom), note the significantly enlarged cardiac silhouette.

control their HF. Individual teaching sessions, covering such topics as low sodium diets, weight and blood pressure monitoring, and exercise programs help prepare patients to deal with their condition on an ongoing basis. This increased knowledge, coupled with the continued support of the NPs, helps ensure that the patients have an improved quality of life while dealing with HF. For more information on the Queen's Heart Failure Disease Management Program, please email heartfailure@queens.org

AORTIC VALVE STENOSIS

The aortic valve, which connects the left ventricle with the aorta, is the most commonly diseased heart valve next to the mitral valve. The narrowing of the aortic valve—aortic (valve) stenosis (AS)—is the most frequent abnormality of the valve.

Although some cases of AS are congenital due to bicuspid aortic valves, the vast majority is acquired by a disease process usually taking decades. This degeneration process caused by aging is comparable to atherosclerosis and the development of coronary artery disease. Hence, degenerative calcific AS is a disease of the elderly, frequently seen in the age group of over 70 years.



Normal aortic valve (left) and stenotic, degenerated and calcific aortic valve (right).

Symptoms may occur with the development of severe AS, which is defined as a valve opening area of $<1 \text{ cm}^2$ (normally greater than 2.5 cm^2) and a gradient across the valve greater than 40 mmHg. These indicators of severe AS are a consequence of the inability of the left ventricle to eject blood to maintain sufficient cardiac output. Classic symptoms of aortic stenosis are dyspnea, angina, or syncope. Once “symptomatic, severe AS” has been diagnosed, prognosis is poor, with annual rates of sudden cardiac death over 15% and an average life expectancy of two to five years.

Aortic valve replacement (AVR) surgery, the mainstay of therapy for AS, is indicated for symptomatic patients. No medical therapy is available to either slow down progression of AS or treat symptomatic severe AS. Isolated AVR surgery is a safe procedure. “The published mortality rate of isolated AVR is 1%,” says Dr. Jeffrey Lau, Cardiothoracic Surgeon at Queen’s Heart. He continues, “In selected patients, this surgery can even be done safely in octogenarians.” However, in some patients with significant comorbidities, risk for AVR may be prohibitively high. In those patients, percutaneous balloon aortic valvuloplasty is a viable option. During this procedure, a large balloon is inflated within the stenosed aortic valve, usually doubling the aortic valve area. The downside of aortic valvuloplasty is its high restenosis rate of over 50% within 6-12 months. Nevertheless, “in selected patients, balloon aortic valvuloplasty may be a good palliative option,” explains Dr. Lee Guertler, Interventional Cardiologist at Queen’s Heart.

More recently, balloon valvuloplasty has evolved into transcatheter aortic valve implantation (TAVI). During this procedure, following regular valvuloplasty, an aortic valve, mounted inside a stent the size of the aortic root, is implanted inside the patient’s native aortic valve, effectively replacing it. The technique has been tested since 2002 and been used in over 15,000 patients worldwide. In the United States, a randomized controlled trial evaluating TAVI in high risk patients has been completed and results are pending.



Bioprosthetic (left) and mechanical (right) heart valves for aortic valve replacement surgery.

CONVENTIONAL CORONARY ANGIOGRAPHY

By accident, coronary angiography—the visualization of the coronary arterial tree by direct injection of contrast—was first performed by Dr. Mason Sones at Cleveland Clinic in 1958. Until then, it was thought that direct injection of contrast in the coronary artery would result in cardiac arrest. Cardiac catheterization and coronary angiography became a therapeutic procedure in 1977 when Dr. Andreas Grünzig performed the first percutaneous balloon angioplasty procedure in Zürich, Switzerland.

Today, coronary angiography and percutaneous coronary interventions are routine procedures. Nationally, over one million coronary angiograms and more than 500,000 coronary interventions are being done. In Hawai‘i, Queen’s Heart is the largest center for this specialized procedure. Cardiac Invasive Services performs over 2,400 diagnostic cardiac catheterization procedures and nearly 600 percutaneous coronary interventions per year. The Queen’s Heart Cardiac Invasive Services Department consists of four state-of-the-art cardiac catheterization laboratories, each featuring the latest digital cardiac imaging technology. Three of the catheterization laboratories are single-plane systems, and one is a bi-plane laboratory, allowing simultaneous imaging of the coronary system in two projections.

Although coronary angiography is very safe with a major complication rate of well below 1%, it remains a minimally invasive procedure. As further outlined in the article about cardiac CT and

MRI in this issue of Heartbeat, non-invasive coronary computed tomography has emerged as a possible alternative to conventional coronary angiography. Both techniques have advantages and disadvantages. In some situations, conventional coronary angiography has clear advantages, such as the ability to carry out a therapeutic coronary intervention during the same setting. In other settings, however, the jury is still out as to which type of angiography—conventional or CT-based—is preferred.



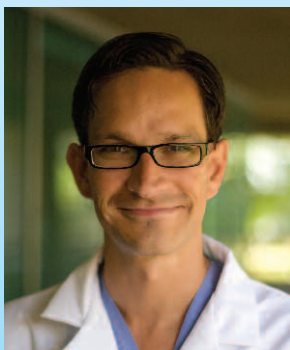
Control room of a cardiac catheterization laboratory at Queen's Heart Invasive Services

MEET THE EXPERTS



DR. CHARI HART

A graduate of Kalani High School and a former University of Hawaii (UH) Rainbow dancer, Dr. Chari Hart earned her medical degree at the John A. Burns School of Medicine (JABSOM) at the University of Hawai‘i. Following her internal medicine residency at the Mayo Clinic in Rochester, Minnesota, she completed a two-year Cardiovascular research fellowship through the National Institutes of Health, and later continued a three-year fellowship in Cardiovascular Disease and Level 3 Echocardiography training at the renowned institution. In 2004, she joined Cardiac Non-Invasive Service at Queen’s Heart Physician Practice. She is also an assistant clinical professor at JABSOM’s Department of Medicine. Dr. Hart specializes in clinical cardiology and echocardiography, with special interest in valvular heart and pericardial diseases. She holds multiple academic achievements and has published numerous manuscripts and abstracts on hypertensive heart diseases, diastolic heart failure, and echocardiography. Outside of work, she spends time with her greatest achievement in life—her family.



DR. CHRISTIAN SPIES

A native of Frankfurt, Germany, Dr. Christian Spies graduated from the University of Hamburg, Germany. After a brief excursion in cardiothoracic surgery, he moved to O‘ahu, where he completed his residency in internal medicine at the University of Hawai‘i. He continued his training in Cardiovascular Disease and Interventional Cardiology with fellowships at Rush University Medical Center in Chicago, Illinois. He returned to the islands in 2008 when he joined the Queen’s Heart Physician Practice.

Dr. Spies specializes in advanced interventional procedures for treatment of coronary disease, structural heart disease, and adult congenital heart disease. He also has an interest in vascular medicine and peripheral vascular interventions. Academically, Dr. Spies has published over 90 abstracts, articles, and book chapters, mainly in the area of patent foramen ovale and atrial septal defect closure, and on topics surrounding peripheral vascular disease. Outside of the hospital, Dr. Spies enjoys spending quality time with his family, and appreciates all sorts of wind-related watersports.

Queen's Heart Update

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Cardiac MRI Study to Evaluate Mechanism of Heart Failure

Crystal methamphetamine (ice) has been identified as a potential cause of heart failure, with the first case report published in JAMA in 1991 by Dr. Robert Hong and colleagues. In a new pilot study funded by the Hawaii Community Foundation, a team led by Drs. Todd Seto and Joon Choi, in collaboration with Dr. Steven Buchthal from the University of Hawaii Magnetic Resonance Imaging (MRI) Research Program, will use cardiac MRI to evaluate patients with methamphetamine-associated heart failure. Specifically, comparing patients with methamphetamine-associated heart failure, patients with ischemic cardiomyopathy, and patients with normal heart function, the team will examine cardiac structure (i.e., left ventricular volume and mass, right ventricular volume and mass, myocardial fibrosis); cardiac function (i.e., left ventricular systolic and diastolic function, right ventricular systolic and diastolic function); and cardiac metabolism (i.e., mid-ventricular myocardial concentrations of creatine, an important compound used in the transfer and storage of energy in muscle tissue) using chemical shift imaging. Enrollment for the study will start this fall.

Research Update from JABSOM

High School Biology Teachers Learned Molecular Biology at the Center for Cardiovascular Research on "Furlough Fridays"

The Center for Cardiovascular Research (CCR) hosted 20 biology teachers from public schools on O'ahu, Maui, and Kaua'i for the last seven "furlough Fridays." Dr. Rachel Boulay, Education Director of the CCR, developed an online curriculum to introduce teachers throughout the state to modern research techniques. She then brought them into the CCR laboratories at the medical school to apply the technologies they learned about in the online program. They performed DNA cloning, Western blotting, and cell culture. An American Recovery and Reinvestment Act supplement grant provided a stipend to make up for the lost salaries on these furlough days, and paid for research supplies for the teachers and travel for neighbor island participants. This program enhances science education in Hawai'i in a highly leveraged manner, as each teacher will take this training back to their classrooms to inspire scores of students. Two of these teachers, Andy Snow of Mililani High and Iris Kahaulelio of Kahuku High, are continuing a more in-depth exposure to research at the CCR this summer working on gene regulation in the heart.



**THE QUEEN'S
MEDICAL CENTER**

