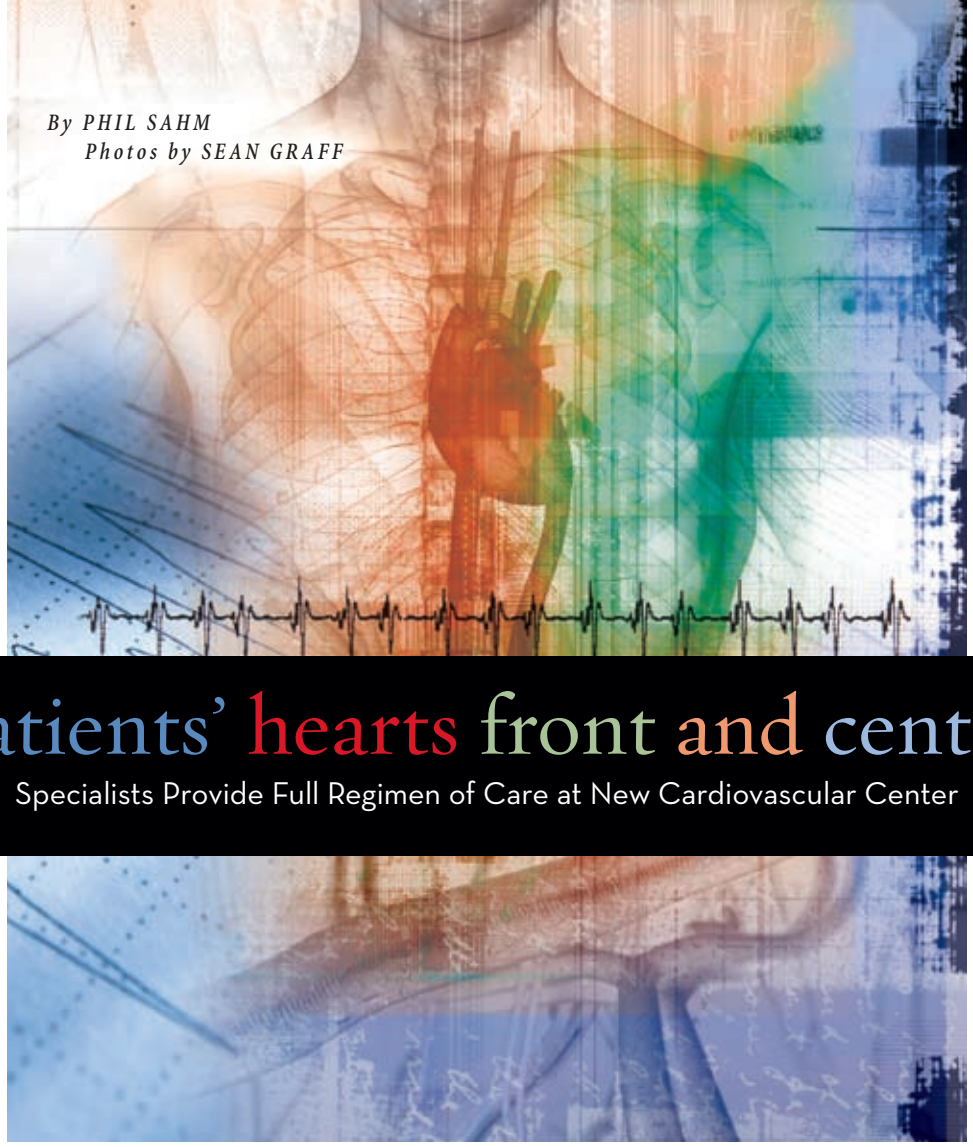


By PHIL SAHM
Photos by SEAN GRAFF

patients' hearts front and center

Specialists Provide Full Regimen of Care at New Cardiovascular Center

Monitoring her arrhythmia **used to take too much of Marjorie Kitchen's time and energy. She would see her cardiologist, Roger A. Freedman, M.D., at University of Utah Hospital. But some of the tests the Woods Cross, Utah, woman needed periodically were available only in a separate clinic in nearby Research Park. If she needed to see another specialist, that required yet another appointment at another clinic.**

That was before University Health Care opened the Cardiovascular Center in University Hospital last fall. A spacious suite of patient exam and special procedure rooms, physician consultation areas, and nursing station, the center brings together specialists who once practiced in separate clinics and seldom interacted with each other into a central location to treat the full spectrum of cardiovascular diseases—from clogged arteries and failing hearts to leaky valves and irregular heartbeats.

STEVE LEITCH

Charles and Marjorie Kitchen

Roger A. Freedman, M.D., and Sheldon E. Litwin, M.D.

Although she's always been happy with her care, Kitchen welcomes the consolidation of services into a single clinic. "I used to go to [University Health Care's] Red Butte Health Center in Research Park to get tests, but would have to see my doctor over in the hospital," she said. "Having everything in a single location makes it a lot easier."

That's an important part of why the cardiovascular center is unique in Utah, according to Freedman, professor of internal medicine at the School of Medicine and the center's medical director. But patients benefit from more than convenience when services are consolidated. Practicing in the same clinic fosters collaboration among doctors, nurses, and technicians from various specialties, so patients receive total care for their cardiovascular-related problems.

"It's the only outpatient clinic in Utah where specialists work elbow-to-elbow in cardiovascular care," Freedman said. "We give a 360-degree evaluation of the patient."

Freedman recalled a recent patient who'd sought a second opinion after being told he needed two operations—one on his carotid artery and another on his heart. Freedman examined the patient, ran tests, and then walked down the hallway to consult with one of the center's vascular surgeons. By the time the patient left the clinic that day, Freedman and the surgeon had determined he didn't need either operation. If cardiovascular services hadn't been in the same clinic, the patient probably wouldn't have had his questions answered so quickly by two specialists.

"I was able to talk with a vascular surgeon in real time, and we coordinated a huge amount in just a few hours," Freedman said. "Next week, I might need to talk with a heart surgeon or interventional radiologist, and they'll be right here."

Ivor J. Benjamin, M.D.

Located on University Hospital's main floor, the cardiovascular center has a staff of 100, including some 30 physicians, specializing in cardiology, heart imaging, vascular and heart surgery, interventional cardiology, and interventional radiology. Tests, imaging, and patient procedures are performed at the center, offering some of the most advanced radiology equipment.

Ivor J. Benjamin, M.D., professor of internal medicine and chief of cardiology at the School of Medicine, believes the University's cardiovascular center represents an overdue shift in preventing, diagnosing, and treating cardiovascular disease: the nation's leading cause of death. "We just can't keep doing things the same way as before," he said. "The concept here is rather than taking patients to the services, we want to take services to the patients."

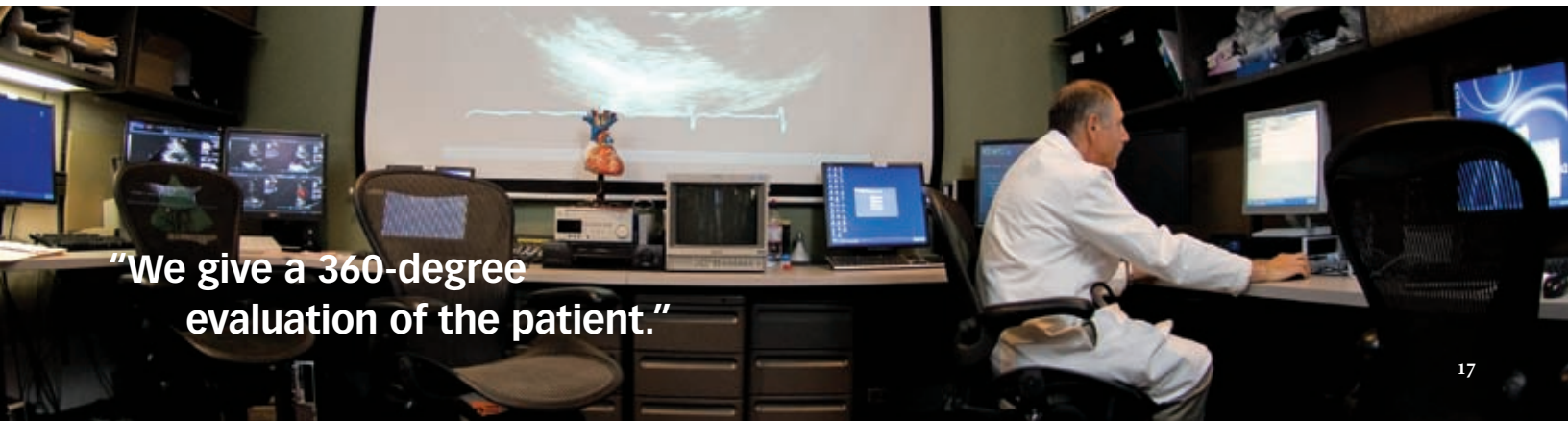
Benjamin, who holds the Christi T. Smith Endowed Chair in Cardiology Research, believes the University's mission as an academic medical center is to find new ways to benefit patients through research and its clinical application. Through affiliation with the School of Medicine and University Hospital, the cardiovascular center meets both missions by giving physicians and other health-care providers access to the latest research, and by offering consolidated clinical services in ways other hospitals can't, according to Benjamin.

He has high goals for the center. "We want this to be the destination point in the Intermountain West for cardiovascular services," Benjamin said. "This is all centered on the patient."

Cardiovascular disease comprises a number of illnesses, including heart disease, stroke, high blood pressure, heart attack, atherosclerosis, coronary artery disease, arrhythmia, angina, high cholesterol, and heart failure. Genetics and lifestyle choices, such as diet and smoking cigarettes, are major contributors to the illnesses.

The cost of cardiovascular disease to the nation, both physically and financially, is enormous. According to the American Heart Association (AHA) 2007 update, one in three U.S. adults—more than 79 million people—has some form of the disease. Utah's incidence of cardiovascular disease mirrors the nation: an estimated one in three Utahns has the disease, which, as the state's leading cause of death, accounts for approximately 4,000 per year.

Long considered primarily a health risk for men, cardiovascular disease strikes and kills more women, new research reports. In 2004, 42.1 million women had cardiovascular disease, compared with



37.2 million men, according to the AHA. In both sexes, the disease is most prevalent among black Americans.

Perhaps not surprisingly, cardiovascular disease adds a staggering cost to the U.S. medical system, with the bill projected to top $430 billion in 2007.

One of the most common types of cardiovascular diseases—and the problem seen most often at the new U of U center—is arrhythmia. It can be caused by coronary artery disease (blockage of the arteries leading to the heart) and damaged muscle from a heart attack. But it also can occur in seemingly healthy hearts. Freedman, an electrophysiologist who studies the heart's electrical system and its effect on the heart rhythm, specializes in treating arrhythmia. That problem, coupled with leaky valves, is what sent patient Marjorie Kitchen to him 11 years ago. When her husband, Charles, started experiencing a drop in his heart rate earlier this year, he became a patient of Freedman's as well.

The University's position as an academic medical center and teaching hospital gives the Kitchens confidence in Freedman, in addition to the other physicians and professionals at the cardiovascular center. "We like the expertise here," Charles said. "The doctors are up on the latest knowledge and procedures. We really wouldn't go anyplace else."

The most common type of arrhythmia is atrial fibrillation: an irregular heartbeat emanating from the heart's upper chambers, which interferes with the electrical signals that foster a normal heart rhythm. Untreated, atrial fibrillation can have dire consequences, inducing blood clots and leading to stroke or heart attack. Depending on the patient, atrial fibrillation is treated through medication, electric shock to restore a normal rhythm (defibrillation), or catheter ablation. Medications include blood thinners to help prevent blood clots and beta blockers to slow the heart rate.

To keep Marjorie Kitchen's heart beating normally, Freedman implanted a pacemaker. Kitchen's heart has a natural tendency to go too slowly at times, and the pacemaker keeps the heart rate up. Other patients have similar devices, implantable defibrillators that not only keep the heart from going too slowly, but also correct heart rhythms that are too fast. Improvements in pacemaker-defibrillators have made the units smaller and more efficient in recent years, and more than 80 percent of Freedman's patients have one of the devices.

Fatty Culprit

Diabetes inflicts major damage *on the cardiovascular system—heart disease and stroke account for 65 percent of deaths in people with diabetes—but exactly how diabetes causes cardiovascular disease is not understood.*

David Symons, Ph.D.

David Symons, Ph.D., associate professor of exercise and sport science at the College of Health, wants to understand that connection. "I'm a vessel guy," said Symons. "I want to determine mechanisms responsible for the effects of diabetes on the body's vasculature system."

He suspects ceramide, a fat molecule associated with obesity and insulin resistance—two of the primary risk factors associated with developing type 2 diabetes—has a role in cardiovascular disease. These suspicions have been fostered through Symons' collaboration with Scott A. Summers, Ph.D., and E. Dale Abel, M.D., Ph.D., associate professors of internal medicine, and doctoral candidate Will Holland, all from the U medical school.

Insulin is a hormone made in the pancreas that the body uses to convert blood glucose into energy for cells. Type 1 (juvenile) diabetes occurs when the pancreas can't make insulin. Type 2 diabetes develops when the body becomes resistant to insulin, preventing the hormone from converting glucose into energy. Approximately 95 percent of the nation's estimated 21 million diabetics have type 2 diabetes, leading many researchers and physicians to believe the high fat of burgers, fries, milk shakes, and other fast-food delectables of the American diet is directly associated with developing the disease.

Both types of diabetes are linked with cardiovascular and peripheral vascular disease, with effects ranging from high blood pressure and clogged arteries, which increase the risk for stroke and heart disease, to peripheral limb pain and, in severe cases, amputation when legs, feet, or other areas of the body don't get enough blood.

Ceramide accumulates in cells as a result of people consuming too much saturated fat, according to Symons and other researchers. "We know the level of ceramide is elevated in obese people," said Symons. "Whether that contributes to vascular dysfunction in people with obesity, we don't know."

Recent research has shown ceramide might have another connection to vascular disease by inhibiting production of an enzyme that helps promote healthy blood flow throughout the body. Endothelial nitric oxide synthase (eNOS) is an enzyme that helps produce nitric oxide, a molecule with many roles in the human body, including that of helping blood vessels stay soft and relaxed to provide maximum blood flow to organs and cells. If that connection is proved, it could potentially link high fat, decreased nitric oxide production, and compromised vessel function.

Symons began researching blood vessels in 1996 and has been working on the role of ceramide for nearly two years. Much of his future research will focus on questions surrounding the connection between ceramide and cardiovascular disease.

"I try to contribute a piece of the puzzle," he said. "If I can figure out some of the mechanisms, I'll have contributed a lot."

The Cardiovascular Center—a spacious suite of patient exam and special procedure rooms, physician consultation areas, and nursing station—enables specialists who once practiced in separate clinics to interact easily and frequently. At left, medical director Roger A. Freedman, M.D., consults with Sheldon E. Litwin, M.D., who heads cardiac imaging.

Nassir Marrouche, M.D., directs the atrial fibrillation program.

A major breakthrough in treating atrial fibrillation recently was defined by Nassir Marrouche, M.D., and his partners at the Cleveland Clinic Foundation. Now an assistant professor of internal medicine and director of the University of Utah's electrophysiology laboratories and the atrial fibrillation program, Marrouche said atrial fibrillation finally can be treated and cured through catheter ablation, which burns damaged muscle causing the irregular heartbeat. He performs 10 to 12 ablations a week, and 40 percent of his patients come from outside Utah.

The procedure involves inserting small wires through a catheter into veins leading to the heart. The wires have sensors to determine which part of the heart is causing the arrhythmia. When the problematic area is identified, the wires "burn" the damaged muscle to prevent it from interfering with the heart's normal rhythm.

"Almost every patient is a candidate for catheter ablation, especially with the good results we are demonstrating today," Marrouche said. "In three to six months after the procedure, the patient should be able to stop taking [the blood thinner] Coumadin."

Symptoms of cardiovascular disease can be noticeable: fatigue, breathlessness, and palpitations. But when the disease strikes veins and arteries, the signs aren't always evident until an emergency occurs.

Atherosclerosis, a buildup of plaque that occludes arteries and veins—commonly called hardening of the arteries—often is not diagnosed until blood flow is restricted to the heart, brain, abdominal organs, or lower extremities. When that happens, angina (chest pain), heart attack, aortic aneurysms, transient ischemic attacks (small strokes), and leg pain can result.

Larry W. Kraiss, M.D., professor and chief of vascular surgery at the medical school and one of four vascular surgeons at the cardiovascular center, sees a cross section of problems at the cardiovascular center, but atherosclerosis is the most common. "Atherosclerosis is a complex disease and can require several specialists to manage it," Kraiss said.

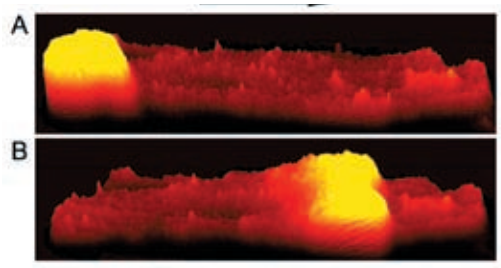
Atherosclerosis occurs when plaque—fatty acids, calcium, cholesterol, and cellular waste products—builds up in the inner lining of medium and larger arteries, causing the artery wall to thicken and decreasing blood flow to the heart, brain, and other organs. The drop in flow can cause heart attack or sudden cardiac death. When blood flow to the brain is decreased through blockage in the carotid artery, strokes can occur.

If atherosclerosis affects the wall of the aorta, the body's largest artery and main conduit for moving blood to organs in the abdomen, pelvis, and lower extremities, potentially fatal bulges in the artery lining (aneurysms) can form and then burst. When blood flow to the legs and feet becomes constricted (peripheral vascular disease), leg pain and even gangrene can occur. "There is a high likelihood that someone with peripheral vascular disease has coronary artery disease, too," Kraiss said.

He and other vascular surgeons at the cardiovascular center have a number of options for treating cardiovascular disease, depending on the patient's age, health, and how seriously the arteries are blocked. In many cases, medication and lifestyle changes—quitting smoking and getting regular exercise—can lessen the problem. Some patients are helped with stents: titanium coils that are placed in the artery,

Larry W. Kraiss, M.D., is chief of vascular surgery.

Steady the Beat



A calcium wave in a heart cell is shown as it moves from left to right.

Every beat of a human heart *begins when "pacemaker" cells in the heart's upper right chamber (right atrium) spontaneously fire electrical signals called action potentials.*

Kenneth W. Spitzer, Ph.D.

Within milliseconds those signals spread like a wave through the heart's millions of cells, and in response to this wave, the heart contracts and pumps blood to the lungs and rest of the body.

Normally, this process produces a flawless heartbeat as electricity moves from cell to cell. If the electrical signal gets interrupted, the graceful rhythm of a heartbeat suddenly becomes irregular, beating too fast or too slowly or not at all. These disruptions in the heart's electrical activity, called arrhythmias, affect millions of people and range from a few benign extra beats to ventricular fibrillation, a life-threatening condition in which the heart stops pumping.

Kenneth W. Spitzer, Ph.D., professor of physiology and director of the University's Nora Eccles Harrison Cardiovascular Research and Training Institute (CVRTI), has dedicated his career to understanding how heart cells generate electrical signals and how these signals malfunction to cause arrhythmia. In particular, he focuses on cellular activity, internal calcium, and pH (level of acidity).

Proper interaction between electrical events and internal calcium is vital for normal heart contraction. As the electrical wave moves rapidly through the heart, it triggers the release of calcium stored inside the cells, causing them to contract. However, vital as it is to a healthy heartbeat, calcium can be too much of a good thing.

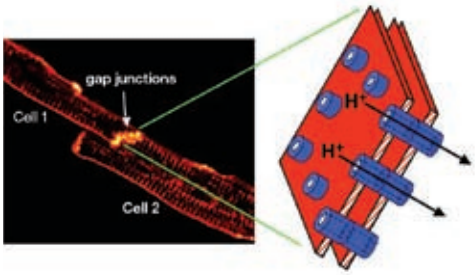
"If the calcium level is too high, it can interfere with electrical activity and cause arrhythmias," Spitzer says. "For example, too much calcium inside the cell can produce calcium waves, which will trigger arrhythmias."

The ability of the heart to generate electrical signals, regulate calcium, and contract is strongly affected by the pH of fluids inside and outside of the cells. During a heart attack the pH of the affected area becomes markedly acidic. This is a key factor in arrhythmias and severely impairs the strength of heart contractions. Spitzer and his colleagues Drs. Richard Vaughan-Jones and Pawel Swietach at Oxford University seek to better understand the mechanisms whereby heart cells control their pH.

It has been known for some time that cells have "proton pumps" that expel acid out of the cell when internal pH becomes too acidic. A key new finding of their research, recently published in Circulation Research, *is that gap junctions provide another major route for acid removal. These are special ion channels that provide cell-to-cell communications in the heart, including the spread of electrical activity. This discovery represents a novel model for cardiac pH regulation in which "proton pumps" and gap junctions work in concert to expel acid from the cell.*

"Our future goals are to investigate the role of gap junctions in pH regulation in both the intact heart and in specialized areas of the heart," Spitzer said.

Spitzer, who has conducted research at the CVRTI and taught students at the School of Medicine for more than 25 years, has been recognized in this country and abroad for his work. The National Institutes of Health has awarded him continuous, peer-reviewed research grants for more than 20 years, including a prestigious MERIT Award (Method to Extend Research in Time), giving him an extra five years' funding for research. In August 2006, Oxford University named Spitzer a visiting professor of cardiac cellular electrophysiology, in large part because of his long-standing research collaboration with Vaughan-Jones.



Gap junctions connect heart cells and provide a key pathway for flow of acid out of the cells.

then expanded to open the blockage. Balloon angioplasty, in which balloons are inflated inside the artery to expand the opening, is another treatment option.

Treating aortic aneurysms used to require major surgery involving weeklong stays in the hospital. Now, many aneurysms are treated using less-invasive endovascular grafts, which can be inserted through small incisions, with hospital stays lasting only one to two days.

Even when a complex vascular problem does require surgery, the "hard-wired" collaboration between the different cardiovascular specialists working together in the same clinic can streamline an otherwise complicated treatment program, because many patients have more than one vascular condition that needs attention. No matter what combination of cardiovascular problems a patient may have, specialists at the U of U Cardiovascular Center can confer and collaborate to find a solution, according to Kraiss. "The goal is to provide a seamless experience for the patient," he said. "We want the patient to leave the cardiovascular center with answers, not yet another appointment to go to another clinic on another day."

Sheldon E. Litwin, M.D., looks at cardiovascular disease from a unique angle: through images that show the disease from the inside out. A professor of internal medicine, Litwin heads cardiac imaging in the Division of Cardiology and provides the expertise critical for other surgeons and cardiologists to diagnose and treat the many types of cardiovascular disease.

"We can look for basically every kind of cardiovascular problem that exists," said Litwin, who holds the Margaret A. Amundsen Endowed Professorship. "The beauty of imaging is that it's non-invasive. There's little or no risk, and it's fast and repeatable."

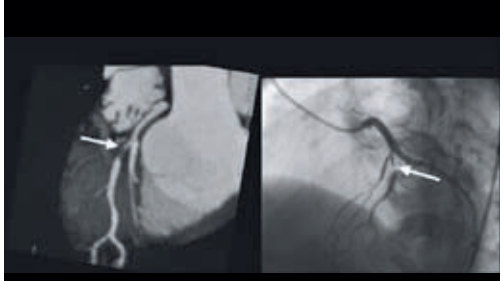
Remarkable advances in imaging the heart and arteries provide information unattainable a few years ago, according to Litwin. The University's newest computed tomography (CT) scanner, uses dual sources of X-rays to produce ultra-fast pictures of the heart, allowing it to capture a 3-D image of the entire heart in a single breath hold (approximately 10 seconds). The Definition™ scanner helps assess plaque buildup in the arteries

that supply blood to the heart muscle, look inside stents to see if they're open, and provide 3-D images of the heart that are used during ablation procedures. Slower CT scanners also can image the heart and coronary arteries, but this usually requires patients be given beta blockers to slow their heart rates. Most patients don't need medication prior to cardiac scans using the dual-source CT. The new scanner also offers another major advantage: it exposes patients to less radiation, because it takes images so quickly, Litwin said.

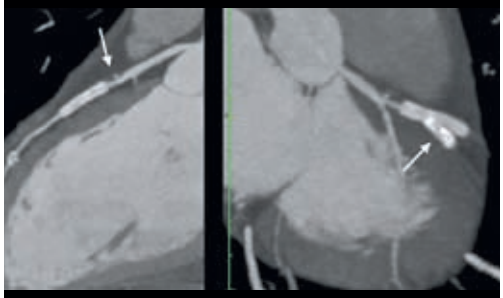
Better imaging means physicians can address cardiovascular problems without invasive procedures. Litwin recently saw a patient in his 60s who was experiencing chest pains. A CT scan showed extensive calcification in the arteries leading to the man's heart. After speaking with the patient and his primary care doctor, they tailored a medication plan specifically for the patient without the need for an invasive procedure.

"By precisely measuring the amount of small calcium deposits that build up in the walls of all three coronary arteries, we can get a very good idea of the total burden of coronary atherosclerosis," Litwin said. "This measure, called a coronary calcium score, is much better at predicting long-term cardiovascular risk than simply assessing traditional risk factors, such as cholesterol levels in the blood."

Surprisingly, more than half the patients who experience heart attacks have cholesterol levels considered normal, according to Litwin, so it makes sense to look at the entire coronary arterial "tree" to determine who really is at risk for a heart attack.



Example of a severe stenosis (narrowing) in the left coronary artery of an asymptomatic patient, which often is referred to as a "widowmaker" blockage. On the left is the noninvasive CT angiogram; on the right, the invasive angiogram. The CT produced findings very similar to the invasive study.



The image on the left shows a CT angiogram from a patient with two stents in the left anterior descending coronary artery. There is a mild plaque in front of the stent, but the stent itself is widely patent (open). The image on the right shows another stent in the same patient that is completely occluded (just after the arrow).

With such sophisticated imaging technology available, the challenge is using the correct imaging test for the problem. The breathtaking advancements in imaging have sprouted an industry of free-standing clinics that pre-screen for diseases. But Litwin emphasizes the U of U Cardiovascular Center doesn't just screen patients, it treats them as well. "It requires more training to determine which test is the right one," explained the cardiologist who has trained at several institutions to learn not just how to use the new technology, but when to use it to gain the best information.

The new imaging technology has opened opportunities in the field of radiology, and Litwin also works with radiology specialists at the cardiovascular center. Their expertise in imaging technology complements cardiologists' knowledge of heart structure, creating a "cross-fertilization" of the two specialties. "I'm very happy with how well we're working together," said Litwin.

As the role of cardiovascular imaging grows, collaboration will become increasingly common in cardiovascular care.

"Physicians treating these patients need information about the structure and function of the heart and cardiovascular system," Litwin said. "Imaging ties the different specialties together." ◩

Color that Counts

Grapes, apples, onions, and broccoli *are more than just colorful. They're also among the healthiest foods to eat, because they contain flavinoids, the compounds that put the red, green, yellow, and other natural colors in food, and provide excellent sources of antioxidants to help protect against heart disease.*

"Any fruit or vegetable that has a lot of color is good for us to eat," says Thunder Jalili, Ph.D., associate professor of nutrition in the College of Health.

Jalili, who researches how food and nutrition affect the heart and cardiovascular system, says antioxidants help the body prevent oxidative stress that could lead to cellular damage. As people breathe and their cells make energy, highly reactive molecules—free radicals—are produced as a response to oxygen. Free radicals travel the body and damage proteins, membranes, and genes through chemical reactions. This damage, oxidative stress, is suspected of influencing a number of diseases, including those in the heart, cardiovascular system, and cancer.

In collaboration with other University health sciences researchers, Jalili studied quercetin (pronounced cor-ce-tin), a flavinoid thought to be an antioxidant that has been shown in studies to reduce oxidative stress in animals. But Jalili found just the opposite: quercetin showed only weak antioxidant properties in rats and none in people.

"Prior studies in rats had shown a reduction in oxidative stress, and we expected to see something similar in people," he said. "But we didn't find any evidence of that."

His research indicated another, unexpected, cardiovascular benefit from quercetin, however: lower blood pressure.

Thunder Jalili, Ph.D.

Jalili mixed quercetin in food and gave it to rats in which high blood pressure was induced. To his surprise, the systolic blood pressure (taken when the heart is beating) dropped 40 points and the diastolic pressure (taken when the heart is at rest) dropped 20 points in the rats with induced high blood pressure. But it had no effect on rats with genetic hypertension.

When Jalili tried a different method to give quercetin to the rats—using a dropper to put it directly into their throats—the blood pressure of those with genetic hypertension dropped as well. In a study with people who took quercetin in tablet form, Jalili found no indication of a reduction in oxidative stress, but did see a 5 percent reduction in systolic and diastolic blood pressure.

The findings from Jalili's studies are congruent with other research showing quercetin may help lower blood pressure in rats by reducing the activity of angiotensin converting enzymes (ACE). These enzymes help produce Angiotensin II, a chemical that causes blood vessels to narrow and can contribute to high blood pressure. If production of ACE is reduced, it can help lower blood pressure. However, it still is unknown whether the same mechanism can occur in humans taking quercetin supplements.

Cardiovascular disease accounts for an estimated 40 percent of U.S. deaths, and diet and nutrition have an undisputed impact on the nation's health. High cholesterol, high blood pressure, diabetes, clogged arteries and other cardiovascular problems all are affected by people's eating habits, according to Jalili.

"So much of the problem is caused by people just eating junk," he said.