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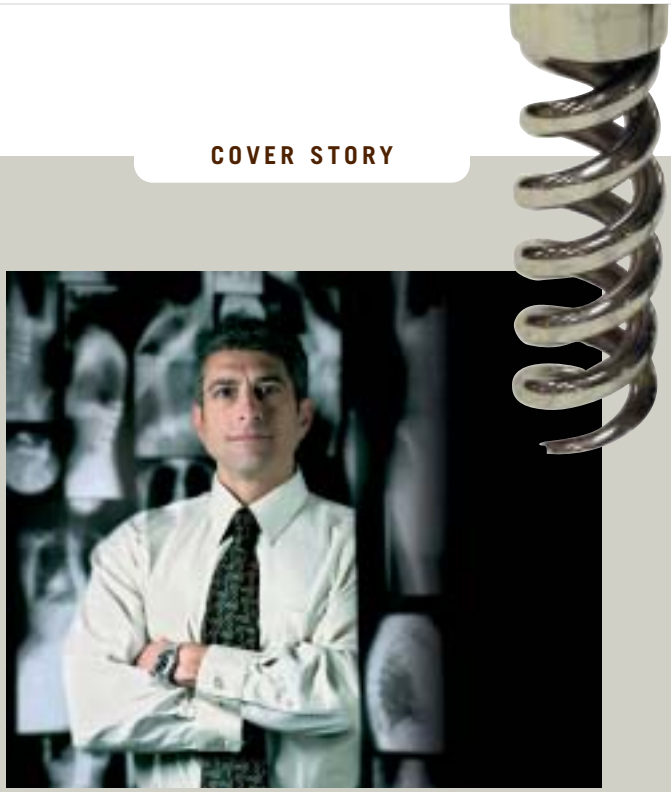


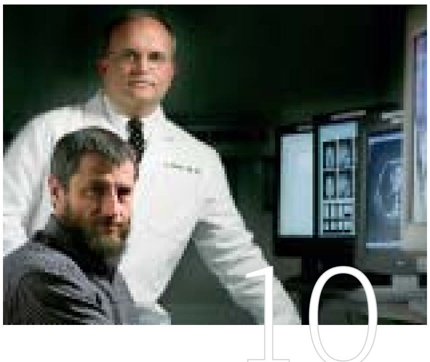
COVER STORY

FROM VISION TO INVENTION **16**

Innovations can come from the most common of objects – sometimes a corkscrew is all you need. Here's how physicians and researchers take their ideas from the lab bench to the patient bedside and, in the end, give us all a healthier future.

ON THE COVER: Merlot Bone Anchor

Features



In This Issue

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NEW LEADERSHIP FOR THE FUTURE

I have been honored to serve as chairman and CEO of The Cleveland Clinic for 15 years, during which time the institution has made critical progress in its goal of becoming America's leading academic medical center. In October, 2004, I will be handing my administration over to a new chairman and CEO, Toby Cosgrove, M.D., who is currently co-director of the Cleveland Clinic Heart Center and chairman of the Department of Thoracic and Cardiovascular Surgery. An outstanding administrator and a distinguished surgeon, Dr. Cosgrove has done much to earn the Cleveland Clinic Heart Center its number one ranking year after year in *U.S. News & World Report's* annual "America's Best Hospitals" survey. As a researcher and educator, he has published more than 400 papers, co-authored a book, authored numerous book chapters, and produced 17 training films. In addition, he has spoken at more than 100 meetings and conferences. He is a true leader with proven abilities.

It is altogether fitting that the new chairman and CEO be one of the many outstanding physicians at The Cleveland Clinic who is strongly associated with excellence in cardiac care. Among the challenges Dr. Cosgrove faces will be the realization of a project that will have a major impact on our institution in coming years – the building of a new Cleveland Clinic Heart Center. The largest single-purpose medical building in the world, the new Heart Center will be an expertly designed complex that will house a cardiac hospital, ambulatory services, advanced surgical and diagnostic capabilities, laboratories, physician support facilities, and patient and visitor amenities. We believe that the new Heart Center will be the right building at the right place and time to meet the growing challenges of heart disease in America.

The need for this facility is urgent. Heart disease is already America's deadliest and most disabling malady. The next two decades will see an overwhelming rise in new cases, as the largest age group in United States' history enters the most at-risk demographic. It is a crisis on our doorstep. The new Heart Center will expand our ability to care for heart patients and their families, grow our opportunities to test new therapies and find new cures, and provide the space, tools and amenities we need to fulfill our role as America's leading heart center.

The campaign for the new Heart Center is now under way. There is no more pressing item on our institutional agenda. The success of this campaign and the completion of this new facility are crucial to more than the future of heart care. As heart services are consolidated in the new building, an enormous amount of space will become available in existing facilities, allowing us to expand other vital medical services, including our growing Neurosciences Center and The Children's Hospital.

The first phases have begun. The cardiac rooftop project is complete for the interface between the old and new buildings. A new office-garage building is under construction on Euclid Avenue, along with a pedestrian tunnel linking it to the main campus. The next phase, abatement of the existing garage, will begin in late 2004, followed by construction of the technology and outpatient areas and the cardiac hospital. The opening is scheduled for early 2008.

The effect of the new Heart Center will be felt across Northeast Ohio and throughout the state. In the most direct sense, it will give the people of this region access to the best heart care in the world in the most advanced facility of its kind. Economically, our expanded services will create new jobs, enrich local businesses and boost local tax revenues. Surrounding communities and institutions will benefit from the halo effect.

As a landmark of world-class medicine, the Heart Center will strengthen the region's already substantial biomedical technology industry. It will spin off new products, create new businesses and help make Northeast Ohio a magnet for new and relocating biotechnology enterprises.

We have undertaken a $300 million campaign in support of this remarkable enterprise, and have been overwhelmed by the generosity of individuals, corporations and the government on its behalf. These advocates share in our belief that the new Cleveland Clinic Heart Center will be the most dynamic center of heart care activity in the world and represents America's best hope for conquering heart disease.

Floyd D. Loop, M.D.
Chairman and Chief Executive Officer

NEW CEO AND CHAIRMAN NAMED

On June 2, 2004, Toby Cosgrove, M.D., was named to succeed Floyd D. Loop, M.D., as CEO and Chairman of the Board of Governors. A distinguished surgeon, accomplished inventor, highly respected researcher and educator, and chairman of the most honored Department of Thoracic and Cardiovascular Surgery in America, Dr. Cosgrove has been described by Dr. Loop as "a real leader, a proven leader," and "someone who can elevate The Cleveland Clinic to new heights." Dr. Cosgrove will be taking office in October 2004. Cleveland Clinic Magazine *is proud to introduce our readers to this remarkable physician and administrator.*

Toby Cosgrove, M.D., learned early in his career that mending hearts is more than cutting and suturing. It is about the importance of striving for excellence, too.

"As we strive to extend people's lives, we must also remember to reach for a higher level of achievement than we ever imagined," says Dr. Cosgrove, chairman of Thoracic and Cardiovascular Surgery, and soon-to-be chairman and CEO of The Cleveland Clinic.

From his youth, Dr. Cosgrove was encouraged to choose a vocation that contributes to the well-being of others. "You could look after people's property, you could look after them spiritually, or you could look after their bodies," says Dr. Cosgrove, recalling his family's values.

While a senior at the University of Virginia Medical School in Charlottesville, one of his professors offered him the opportunity to study under renowned cardiac surgeon, Robert Gross, M.D., then chairman of surgery at Boston Children's Hospital and the first person in the world to operate on the cardiovascular system.

"He was a giant among men," recalls Dr. Cosgrove.

While there, he was inspired by the need to develop more effective methods in cardiovascular surgery. "I remember the surgical service losing five children one day. It was a sobering experience." It impressed upon him the importance of reaching for something that hasn't yet been achieved, "the importance of pushing the frontier forward to one day offering patients more than we can today."

Dr. Cosgrove's experience continued as a physician stationed in Da Nang, Vietnam. At a casualty staging center, in just nine months, he and one other surgeon triaged and treated 22,000 men.

Toby Cosgrove, M.D.

"This experience not only taught me aspects of medicine I couldn't have learned in the most modern medical facilities," Dr. Cosgrove noted, "but also that one can be successful even under the worst of odds."

Upon discharge, he was accepted at Massachusetts General Hospital in Boston for his residency and served as chief resident in cardiac surgery at Boston Children's Hospital.

In 1975, he was recruited to The Cleveland Clinic as a staff member. He succeeded Floyd D. Loop, M.D. as chairman of Thoracic and Cardiovascular Surgery, when Dr. Loop was named chairman of the Board of Governors of The Cleveland Clinic.

In the following years, Dr. Cosgrove continued to pursue the science of medicine.

Over the course of his career, Dr. Cosgrove has performed more than 18,000 surgical procedures and has become a world-renowned expert in the field of heart valve repair. He has developed and filed 19 patents, including the Cosgrove Mitral Valve Retractor, the Stentless Aortic Valve, Low Velocity Aortic Cannula and the Cosgrove-Baxter Annuloplasty System for use in valve repairs.

"You keep looking at a problem and trying to figure out a better way to solve it," says Dr. Cosgrove. "I try to instill that same high level of expectation in the residents in my department. We openly state, in fact, that we are training the next generation of leaders in cardiothoracic surgery."

Dr. Cosgrove is a highly respected researcher and educator. He has been an invited lecturer or honored guest speaker at hundreds of national and international symposia, conferences and meetings. He is a member of several editorial boards including the *Annals of Thoracic Surgery*, *Journal of Heart Valve Disease*, *American Heart Journal*, *Circulation* and *Cardiac Chronicle*, among others that include journals in Italy, Kuwait and Germany. He has published nearly 400 papers, co-authored a book, authored numerous book chapters, and produced 17 training and continuing medical education films.

Today, Dr. Cosgrove is confident as he assumes the office of chairman and CEO of The Cleveland Clinic. "The Cleveland Clinic is a haven for patients from around the world," he says. "No other health care institution is better prepared to meet the challenges of the 21st century."

LETTERS TO THE EDITOR

Our first issue generated many positive responses from our readers. Here are a few.

Kudos

Just a quick email to tell you how impressed I was with the new *Cleveland Clinic Magazine*. It was insightful, engaging, educational, inspiring. The photo quality was excellent... articles well done...diversity of topics... all in all a great piece. Not only was it interesting to read...it really does make you proud of the Clinic and generates a great desire to want to support the good work you are doing. Congratulations! I look forward to future issues.

Bob Stec
(received by email)

Excellence in Sight

Congratulations on the new *Cleveland Clinic Magazine*. I read with interest the story by Natalie Manco ["An Independent View"]. I trained a year behind Dr. Rockwood, and agree that he is an excellent clinician in ophthalmology and glaucoma. I also had the honor to train under the auspices of Dr. Langston, one of the superb ophthalmic surgeons at the Clinic. I understand why Natalie has done so well with her glaucoma and corneal work. It is a pleasure to receive the Clinic publications to keep in touch. Every day I am thankful to CCF for the strong training program. Keep up the good work!!

Joyce H. Cassen, M.D. (Oph 85)
Honolulu, Hawaii

Bedazzling

Brava! I am bedazzled by your first issue. From format to photography to informative content, this instrument will give CCF a leg up in polishing its already superior image. Keeping readers updated on the cutting edge of medical progress is a valuable contribution...May you have many years of great success.

Barant "Barry" Downs
Ann Arbor, Michigan

If you would like to comment, send email to:
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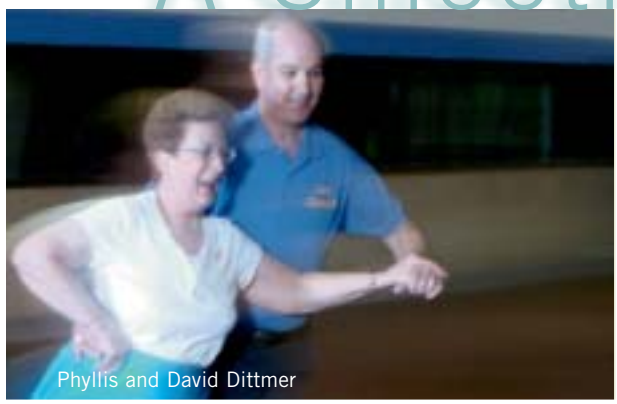
A Smooth Glide


Phyllis and David Dittmer

They first met at a roller-skating rink. Six years and two knee replacements later David and Phyllis Dittmer of Amherst, Ohio, are still skating. Five years ago Michael Kolczun II, M.D., a surgeon with the department of Orthopaedic Surgery, performed a unicompartmental, or "partial," knee replacement, on David's right knee. Four years ago he performed the same procedure on Phyllis' right knee.

The knee is the body's largest joint, comprised of the lower thighbone, upper shinbone and kneecap; damage to the cartilage cushioning these bones means they no longer glide together smoothly. Bending and straightening the leg to walk, to climb steps – and to roller skate – causes painful friction. "When my knee locked up, the pain was unbearable," Dittmer recalls.

The cartilage in David's knee had deteriorated after an in-line skating injury and surgery was called for. Total knee replacement would dramatically improve Dittmer's quality of life, but he had a larger concern. "Total knee replacement at that time would have made my knee operate like a hinge. That isn't good for skating. You need to be able to twist your knee, to turn your foot."

Dr. Kolczun proposed looking inside David's knee with an arthroscope to determine the extent of the damage. If the damage was confined to just one of the knee's three compartments, partial knee replacement, a less invasive alternative, was an option. About 30 percent of knee replacement patients are eligible for this procedure.

In standard total knee replacement, a 6- to 12-inch incision is made. Surrounding muscles are parted, and surgeons insert a grooved metal component into the lower thighbone, attach a plastic-covered metal implant to the upper shinbone, and cover the kneecap with high-density plastic.

But partial knee replacement requires only a 3-inch incision and leaves surrounding muscles and ligaments undisturbed. Surgeons attach a grooved metal implant to the lower thighbone and a plastic implant to the upper shinbone. The kneecap and any healthy cartilage are preserved, and recovery time is cut in half. Most patients can use their knee shortly after surgery, relying on crutches or a cane for a short period of time as they heal.

"They asked me to stand on my leg at 7 p.m. the day of surgery," Dittmer recalls. "I couldn't believe they wanted me to stand on my right leg so soon." The next day found him maneuvering steps using crutches. "When my wife saw how well I did with my knee, she decided to try it."

A year later, Phyllis had the same surgery where the cartilage had deteriorated and arthritis had developed over the years.

Following partial knee replacement, strenuous activities are typically put off for several months – but the Dittmers were eager to lace up their skates again. "We took it slow at first, skating around the edge like beginners," says David. "We could skate better than we could walk. But once we got back into it, you'd never know we had a problem."

Heart Alert for Women

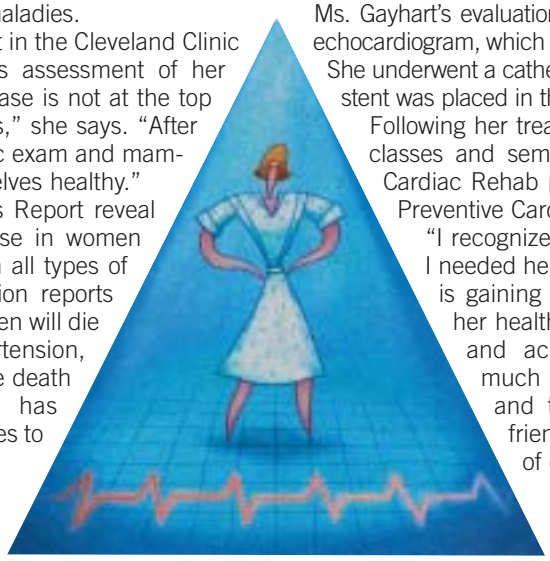
Sammie Gayhart is on a mission. She is talking with women she knows and those she meets casually.

She is sharing her story. She believes it is the best way to make women aware of the risks of heart disease.

Like most women who experience the symptoms of heart problems, Ms. Gayhart wrote it off. "I had reflux and a hiatal hernia, so I assumed that is why I had indigestion," she recalls. "And, of course, I was fatigued. But what woman isn't tired these days with all that we are doing?" Symptoms for women differ from those in men and are easily attributed to other maladies.

Ellen Mayer Sabik, M.D., a cardiologist in the Cleveland Clinic Heart Center, says that Ms. Gayhart's assessment of her symptoms is pretty typical. "Heart disease is not at the top of most women's list of heath concerns," she says. "After they get a negative report on their pelvic exam and mammogram, most women consider themselves healthy."

Data from the National Vital Statistics Report reveal that deaths from cardiovascular disease in women outnumber two to one the deaths from all types of cancer. The American Heart Association reports that each year more than 500,000 women will die from coronary artery disease, hypertension, stroke and other vascular diseases. The death rate from cardiovascular diseases has decreased among men, while it continues to increase in women.



"Because women tend to ignore cardiac symptoms and often don't recognize them as such, they seek treatment much later than men," says Dr. Sabik. Such was the case with Ms. Gayhart, who admits that she "walked around with her symptoms, thinking they would go away." It wasn't until her son, a surgeon in Bangor, Maine, urged her to see a cardiologist that Ms. Gayhart began to take her symptoms seriously.

Ms. Gayhart's evaluation at the Clinic included a stress test and echocardiogram, which revealed a blockage in her coronary artery. She underwent a catheterization and angioplasty, during which a stent was placed in the coronary artery to restore blood flow.

Following her treatment, Ms. Gayhart continues to attend classes and seminars sponsored by the Heart Center's Cardiac Rehab program and also by the Heart Center's Preventive Cardiology Department.

"I recognized that I had to change my lifestyle, and I needed help to do that," she says, relating that she is gaining the information she needs to maintain her health and is sharing it with friends, relatives and acquaintances. "Women are under so much stress. We are working, raising families and taking care of relatives, employees or friends. We have to make sure we take care of ourselves, too."

SYMPTOMS AND RISK FACTORS OF HEART DISEASE FOR WOMEN

symptoms

1 pain in chest, upper back, jaw or neck
2 shortness of breath
3 flu-like symptoms: nausea or vomiting, cold sweats
4 fatigue or weakness
5 feelings of anxiety, loss of appetite, malaise

risk factors

1 family history of heart disease
2 smoking, diabetes, overweight/obesity
3 high blood pressure
4 sedentary lifestyle
5 diet high in saturated fats
6 high cholesterol

Better Relief for Incontinence

Two years prior to Anne's* appointment with the Cleveland Clinic Glickman Urological Institute, she had undergone an unsuccessful surgical procedure elsewhere to treat stress incontinence.

"If anything, the incontinence was worse following the surgery," Anne says. "I had absolutely no bladder control. It didn't matter what I was doing – whether I sneezed, laughed or coughed. I couldn't lift anything heavy or light. Any activity would trigger it."

Anne is one of an estimated 13 million people, mostly women, who suffer from incontinence. Although many women turn to various absorbent products for relief, too embarrassed to seek medical help, there are a wide variety of medical and surgical treatment options that can restore or improve bladder control.

During her first appointment with Sandip Vasavada, M.D., at the Section of Female Urology and Voiding Dysfunction, Anne's anxiety evaporated. "Dr. Vasavada told me exactly what he was going to do. He explained the urodynamic testing that would be done before the procedure." Urodynamic testing provides information on how well the bladder and sphincter muscles, which control the release of urine, work.

Because Anne had experienced complications from a prior vaginal sling procedure, Dr. Vasavada elected a newer minimally invasive procedure, called the transobturator tape approach, that he believed would be appropriate for her problem.

"The transobturator approach means the sling passes through the obturator canal (the groin creases) as opposed to behind the pubic bone, which is typical of other surgical approaches," explains Dr. Vasavada. "This is truly a minimally invasive procedure, with less trauma to internal tissues."

The transobturator procedure can be performed under local, general or spinal anesthesia. Dr. Vasavada says that most patients, if not all, go home the same day a few hours after surgery and experience minimal pain or discomfort.

Anne says when she woke up from the surgery, she was a little groggy but that was all. Today, she moves around freely, with no concerns. "I feel free to do anything I want. It's unbelievable."

*Name changed at patient's request to protect confidentiality.

Washing Away Cataracts

Warm salt water washing away the clouds. Though it sounds like a tropical vacation, it's actually a new technique for cataract removal, called Aqualase, which uses tiny pulses of salt water to help dissolve certain types of cataracts.

Some cataracts are easier to remove than others. Most form slowly, over many years, turning the once clear layers of the lens in the eye into a hardened, opaque thickness that interferes with vision and requires a good deal of energy to be removed. To break up these more common, dense cataracts, ophthalmologists use ultrasound and heat in a process known as phaecoemulsification.

But for about 10 percent of those with cataracts, this annoying cloudiness is confined to just the thin, outer layers of the lens. For this group, ophthalmologists can now use the less-aggressive Aqualase approach that directs microjets of warm saline at the thin outer layers of the lens – essentially washing the cataract away.

"We are able to remove these cataracts one layer at a time," says Michael Gressel, M.D., a Clinic ophthalmologist who has been doing the new procedure for nearly a year. "The layers are so soft, they offer almost no resistance."

The softer types of cataracts that yield to squirts of saline occur most often in patients for whom the cloudiness develops suddenly and in patients who are under 60 years old.

Newer, more robust versions of the Aqualase procedure may extend its use to about 25 percent of those who have cataract surgery in the United States each year, or about 625,000 people.

And cataracts aren't the only reason that Clinic doctors now use this water-powered device. For those too farsighted (hyperopic) for laser vision correction, doctors now use the Aqualase approach to totally remove the eye's natural lens before replacing it with a lens implant.

The Aqualase water-powered device uses microjets of warm saline to remove the softer type of cataract.

Tennis is Heart Healthy!

Playing tennis on a regular basis can help maintain or improve balance, mobility, agility, strength and fitness. It also helps burn calories. According to Cleveland Clinic Heart Center exercise physiologist and avid tennis player Gordon Blackburn, Ph.D., research shows that three hours of moderate aerobic exercise every week can cut the risk of developing heart disease by 50 percent. "Playing tennis at a moderate to vigorous intensity on a regular basis is a good way to get your aerobic exercise," says Dr. Blackburn. "You'll exercise your muscles and burn calories. Tennis can even help lower your blood pressure. All of that helps reduce your risk of developing heart disease or of having a cardiovascular event, such as a heart attack or stroke."

A 135-pound woman playing an hour of tennis can burn approximately 330 calories during doubles and 420 calories during singles, says Dr. Blackburn. An average-sized man playing an hour of tennis can burn about 425 calories during doubles and 600 calories during singles. In fact, you'll burn more calories playing three hours of tennis per week than you will doing three hours of light weightlifting, bowling or golfing.

Cleveland Clinic donor and tennis enthusiast Shirley Foote strongly believes in the value of playing tennis to keep healthy. Although she didn't start playing until she was 41 years old, at the height of her tennis playing days she was playing every Wednesday for five hours a day. Mrs. Foote also has passed down her love for the sport to her 31 grandchildren. Five years ago, she began arranging weekly tennis lessons for the children, who start when they are five years old and "graduate" when they are 13.

"I can't say enough for having a healthy heart and playing tennis," says Mrs. Foote. "When I play, I feel stronger, healthier and enjoy my whole life more."

GET YOUR GAME ON...SAFELY

Dr. Blackburn encourages anyone who can to take up tennis. But certain individuals, he says, need to check with a physician before doing so. If you are interested in playing tennis, check the list below to see if any of the criteria describe or relate to your health status. If so, you'll want to speak to your doctor first.

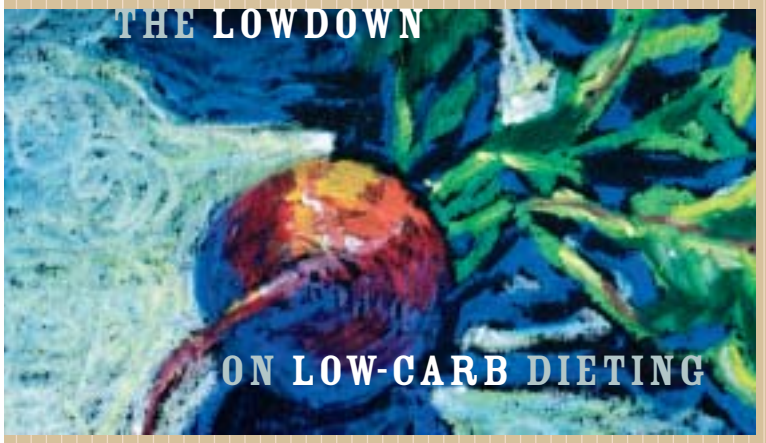
- *Chest, neck, jaw or arm discomfort or pain during physical activity*
- *Shortness of breath or unusual fatigue at rest or with mild exertion*
- *Leg discomfort with exertion*
- *Skipped or rapid heart beats*
- *Regular dizziness or loss of consciousness*
- *Vision problems*
- *History of chronic joint pain or discomfort that worsens during physical activity*
- *Cardiovascular disease (cardiac, peripheral arterial or cerebrovascular disease)*
- *Pulmonary disease*
- *Metabolic disease (diabetes, thyroid disorder, renal or liver disease)*
- *Recent surgery (within past year)*
- *Pacemaker*
- *Rheumatoid arthritis*
- *Osteoporosis*
- *Joint replacement*

Individuals at high risk for developing coronary artery disease should also check with their physician before taking up tennis. High-risk individuals are men over 45 years of age and women over 55 years of age with two or more of the following conditions:

- *Family history of heart disease before age 55*
- *Current smoker or quit within the past year*
- *Resting blood pressure >130/>85 mmHg*
- *Elevated cholesterol (total cholesterol >200 mg/dl or LDL cholesterol >130 mg/dl)*
- *Impaired fasting blood sugar (fasting glucose>100 mg/dl)*
- *Obesity (Body mass index > 30 or waist girth >39 inches)*
- *Sedentary lifestyle (<30 minutes of moderate physical activity on most days of the week)*

Also, if you are under a physician's care for any reason, or taking medications to help manage a condition, be sure to discuss with your physician your interest in tennis before heading off to the courts.

TO HELP YOU APPRECIATE THE HEALTH AND HEART BENEFITS OF TENNIS, TO ENCOURAGE YOU TO GET OUT THERE AND PLAY, AND TO HELP YOU PLAY THE SPORT SAFELY, THE CLEVELAND CLINIC AND THE UNITED STATES TENNIS ASSOCIATION HAVE JOINED TOGETHER TO PROMOTE TENNIS AS A HEART HEALTHY SPORT. FOR MORE INFORMATION GO TO WWW.TENNISWELCOMECENTER.COM.



High-protein, low-carb diets have become the new mantra for weight loss in America. An estimated 32 million carb-conscious Americans are overhauling their meals with tenets from the well-known Atkins and South Beach diets, which forbid or severely limit eating bread, pasta, potatoes and other starches. These diets also blacklist refined flours – so out go the sugary sweets such as cookies, donuts, cakes or candies.

One effect is that Americans now spend about $2.5 billion a year on low-carb products in hopes of shrinking their waistline, while keeping their food choices ample. As the food industry's big-money marketing machines stuff hundreds of new, low "net" carb items on supermarket shelves, the beleaguered orange juice and potato food industries, to name a few, rush to re-position their products as healthy "smart carbs."

But can anyone say if these diets are really good for us?

Studies Needed The original Duke University study that kicked off the current fad only assessed dieters over a six-month period. That's not a very long time for something that could potentially affect the rest of your life.

"Nobody knows the long-term effects since it hasn't been carefully studied," says Eric Topol, M.D, chairman of Cardiovascular Medicine. "It's all about total calories and good versus bad carbohydrates. So you're taking a risk if you, and your diet, don't take these points into account."

New studies are being launched that will examine the low-carb diet's long-term effect on weight, arteries, cholesterol, body composition, bones and kidneys. But the verdict is still out. There are, however, some things we do know.

"Long-term scientific evidence has proved that foods like fatty cuts of meat, cheese, cream, and butter – allowable foods on the Atkins diet – are all high in saturated fat and cholesterol," reports Melissa Stevens Ohlson, M.S., R.D., L.D., nutrition program coordinator in Preventive Cardiology and Rehabilitation. "These are the same foods associated with increases in blood cholesterol and risk for heart disease."

In addition, foods high in saturated fat have a direct impact on the flow of blood in arteries. Studies conducted on high fat versus low fat meals have shown that the arterial wall is narrowed after a high-fat meal, restricting the flow of blood. If you already have some narrowing of the arteries, this means further constriction of the arteries could potentially lead to a heart attack or stroke.

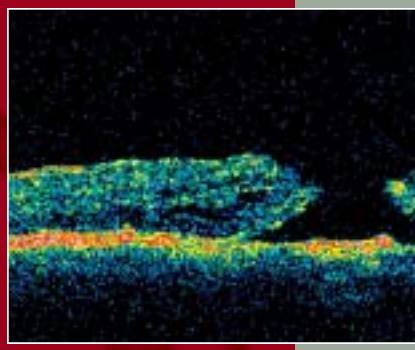
"Conversely, the foods that low-carbohydrate diets discourage are precisely the foods that have been shown to protect the body from heart disease – a variety of fruits, vegetables, legumes [dried beans, lentils, split peas] and unrefined whole grains," states Ms. Ohlson. These foods provide the body with necessary vitamins, minerals and phytonutrients that are essential to good health.

Ketones May Be Key "Most of the weight loss in the first two weeks of a low-carb diet is from fluid loss," says Sethu Reddy, M.D., chair of the Endocrinology Department. "This can cause problems like dehydration. And with high-protein, low-carb diets, ketone levels in the dieter's blood goes up. During that process their kidneys excrete more potassium, and the potassium level in their blood drops down to a dangerous level. This has the potential to lead to muscle fatigue and heart arrhythmias."

And scientists aren't sure just how safe this increase in ketone production is. For example, many suspect that it may be detrimental to kidney function because it causes the kidneys to work harder in order to excrete the additional waste. Other researchers question whether the excess protein in low-carb diets might leach calcium from bones, resulting in weakened bones. The salt and water depletion that occurs during ketosis may cause hypotension (low blood pressure), fatigue, fainting, constipation and kidney stones. Others fear excess ketones may impair metabolism of insulin and liver function. And most importantly, we just don't know the impact excess ketones may have on persons who have diabetes, high cholesterol or high blood pressure.

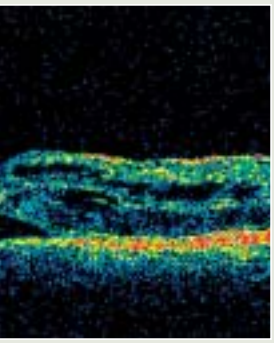
Finally, consider this: most dieters go off a diet at some point – that's human nature. And when the weight returns, they jump back on the dieting bandwagon, returning again and again to the "induction" or the extreme, limited-eating phase of the diet. "Repeated return to the induction phase is like yo-yo dieting," Dr. Reddy explains. "The body's metabolism shifts to become more efficient and conservative – leading to fat gain."

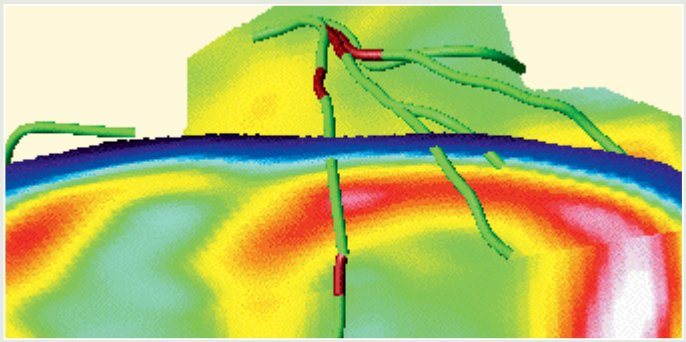
"Nobody knows the long-term effects since it has not been carefully studied." Eric Topol, M.D.

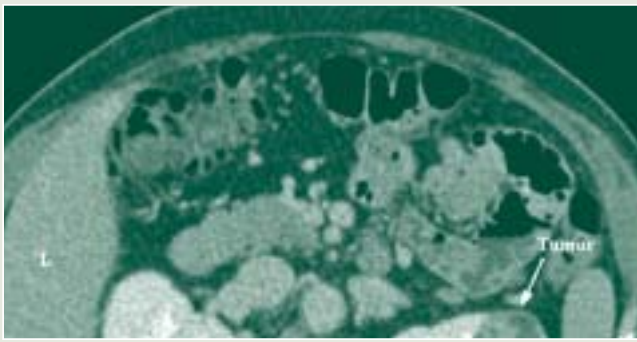


THE BIG PICTURE

Getting a look inside the body has come a long way in the last 100 years. Today the possibilities are endless.







Beth Graham had been to a party the night before the headache began, and at first she thought maybe that was its source – too much of a good time on a Saturday night.

But the headache kept getting worse. The 36-year-old mother went to see her family doctor right away, who figured that Mrs. Graham had a lingering sinus infection and treated her with another round of antibiotics. The headache didn't go away, though: it became so painful that Mrs. Graham couldn't sleep at night and wound up spending hours at the kitchen table crying. She went back to her family doctor, who did an MR (magnetic resonance) image of her sinus area and sent her home with a report of chronic sinusitis.

Still, the terrible headache didn't go away. The following Saturday, less than a week after the headache began, Mrs. Graham stumbled back from the garage with dirt on her face and leaves in her hair. "How long was I out there?" she asked her husband, Michael. "I think I might have fainted."

With that, her husband called someone to take care of their two young sons and whisked her off to the local emergency room. Just after they checked in, Mrs. Graham heard a ringing in her ears and cried out. Her husband turned to see her in the midst of a seizure. She was quickly taken away for an angiogram – an imaging procedure in which a substance is injected into the blood vessels so that twists, turns and abnormalities show up when x-rayed. A neurologist confirmed that two of Mrs. Graham's four major arteries to the brain had aneurysms, while unexpectedly the other two major vessels had collapsed. She and her husband were quickly life-flighted to The Cleveland Clinic where a team of specialists in neurosurgery and neuroradiology were waiting for her.

The team had determined that two potentially fatal forms of stroke had simultaneously struck Mrs. Graham: not only had two arteries collapsed and blocked blood to the brain, but one of the aneurysms had burst. Using a bi-plane angiography–showing two views simultaneously– the team, which was led by Peter Rasmussen, M.D., head of Endovascular Neurosurgery, was able to repair the damaged arteries in her brain in only a few hours through a pencil-wide incision in her leg using real-time image guidance.

"Everything bad happened all at once," says Thomas Masaryk, M.D., the neuroradiologist who was summoned to be part of Mrs. Graham's team that night. "She appeared almost brain dead when she arrived, but through a combination of advanced imaging and less-invasive neurosurgery, as well as Dr. Rasmussen's quick thinking, she is alive and recovering. In my 22 years practicing medicine, this is the closest thing I've seen to a real-life miracle."

Superhero Vision

Many of today's medical miracles stem from advances in imaging, the array of technologies and techniques that allow doctors to peer into the body's innermost workings and spot problems that would have remained a deadly mystery just a few years ago.

Small images above, left to right: Optical Coherence Tomography (OCT) image showing a macular hole in the eye; Positron Emission Tomography (PET) and Computed Tomography (CT) image of a heart; CT scan showing a kidney tumor.

Two kinds of MR images of the same area in this patient's heart show evidence of thinning, but only partial scarring, of the tip of the left ventricle (arrows), indicating enough leftover muscle for a coronary bypass graft.

"We're always at the development forefront," says Michael Modic, M.D., chair of the Department of Radiology. "We're not only using the newest equipment, but we're also helping develop new applications and technologies."

Imaging has come a long way since Wilhelm Roentgen, a German professor of physics, discovered X-rays in his lab in 1895. At first, X-rays were only used to detect broken bones and foreign matter like bullets, but scientists soon learned how to add contrast agents, such as density-characterizing dyes, so that the X-rays could distinguish between different soft tissues. Over the years, machines using X-rays became more powerful and technologically sophisticated.

In the 1970s, the CT (computed tomography) scan was born – and one of the first in the world was tested at the Clinic. In a CT scan, the patient lies on a table and a device containing both the source of X-rays and detectors whirl around the body, collecting images from every possible angle. A computer then reconstructs these images into a three-dimensional perspective of the body. These machines keep getting faster and more accurate as the number of detectors keeps increasing. It now takes 20 seconds to do a full-body scan, whereas it took 40 minutes back in the 1970s.

Imaging techniques using other physical forces – sound, radio waves and now light – have also been added to the arsenal of imaging tools. Perhaps the most stunning advance in recent years comes from the powerful computers harnessed to these various imaging technologies. Instead of capturing images in an analog form, such as photographic plates or film, most of the images are now captured digitally. Radiologists then use software – some of it developed for the first Star Wars movie to create special effects – to post-process the images so they can be manipulated to reveal just about anything the treating physician wants to know.

"Now we have data sets that we can slice and dice any way we want," says Dr. Modic. "We're only limited by our imagination. Working in radiology is like working in a video arcade – it's a great show and leads to great medicine."

Of course, prowess in radiology isn't just due to the sophistication of machines. It's also due to the expertise of the radiologists who use them. Most Clinic radiologists are subspecialized, so they learn to identify problems in their subspecialty area that a general radiologist might not. Since Clinic radiologists conduct some 1.3 million exams every year, they have many opportunities to train their critical eye on small nuances that might yield important information.

Peter Rasmussen, M.D. and Thomas Masaryk, M.D.

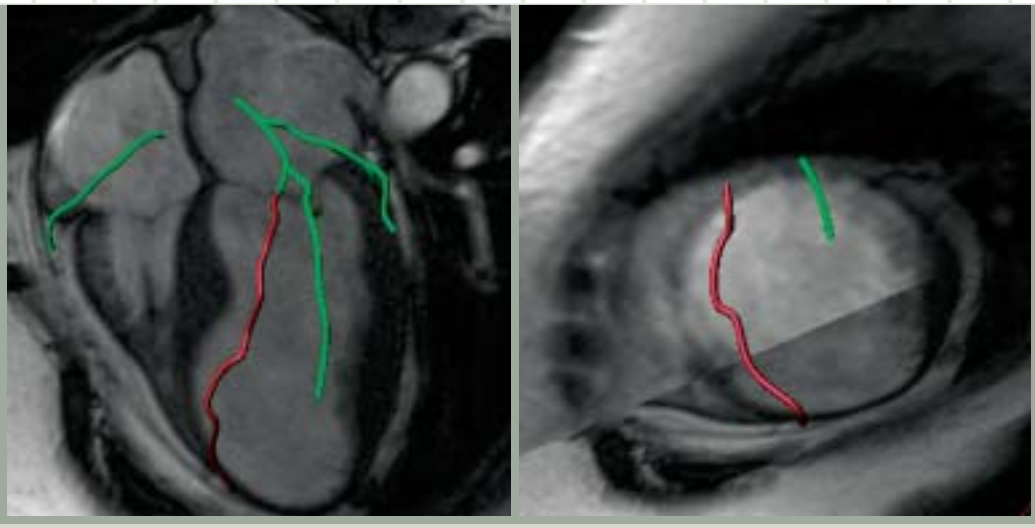
Richard White, M.D. (standing) and Michael Modic, M.D.

Advanced Imaging Key to Advanced Treatment

In one of the Clinic's dimly lit Reading Rooms, radiologists sit in front of computer screens and examine – or read – the results of different imaging methods. Radiologist Brian Herts, M.D., retrieves a digitized CT scan of an abdomen and shows what the post-processing software can do. The CT captured some 500 images, or slices, of the abdomen, and the computer has already put those slices back together to create a seamless image of the body's interior. As Dr. Herts makes the image revolve, it looks as if an anatomical drawing has come to life. He can make the computer assign a different color to each organ so that they're more easily distinguished from each other. He can make the computer zero in on one of the kidney's blood vessels and then "walk" the viewer around that point to examine the blood vessel's connection with the kidney from every angle. He can create a plane that bisects the digitized body from any angle, giving an increasingly deeper view of the entire abdomen, one tiny layer at a time. He can even give the viewer a virtual ride through the person's colon: the computer uses a special perspective, volume-rendering software that allows radiologists to "fly" through the long pink tunnel of patients' colons looking for abnormalities, giving patients a painless "virtual" colonoscopy.

Aside from presenting a great show, these digital models help physicians detect disease and injury and plan treatment. In fact, imaging is key to the success of today's less-invasive and highly sophisticated treatments.

In urology, for example, physicians can now offer patients with kidney cancer a solution other than total kidney removal: a partial nephrectomy, in which only part of the kidney is removed. This is a good option for patients who only have one



A CT angiogram of the coronary artery tree showing open (green) and closed (red) segments is combined with MR images that confirm poor thickening (right image) and severe scarring (far right image) in the area of the heart muscle where the artery has closed.

kidney, as the remaining piece of kidney will work well enough so that the patient won't need dialysis. However, even as this procedure simplifies life for the patient, it complicates the surgeon's work.

"When surgeons do a partial nephrectomy, they need more sophisticated information than if they're taking out the whole kidney," explains Dr. Herts, who specializes in abdominal imaging. "If they're taking out the whole kidney, all they need to know is that the tumor exists. But if they're only taking out part of it, they need to know everything about the blood vessels, the urinary tract, and exactly where the tumor is. That's the kind of information provided by these three-dimensional CT models."

Imaging the Brain

Few medical fields have been as transformed by advanced imaging as neurology and neurosurgery. Only a few years ago, neurosurgeons would have treated a brain aneurysm – a small, fragile blister on the artery that can burst and cause stroke – by opening the skull and attaching a clip to the protrusion. Now, neurosurgeons handle many aneurysms by threading a tiny guidewire into the artery and using it to insert a coil inside the aneurysm. In the past, coils were sometimes inadvertently placed in a spot where they would fall out, often causing a stroke by blocking the vessel. Now that these 3-D CT models give neurosurgeons better information about the exact anatomy of each patient's brain, the surgeons know if they need to add some scaffolding – also called stents – to strengthen the arterial wall before inserting the coil.

"We couldn't do this kind of surgery without high-resolution imaging," says Dr. Rasmussen. "When we treated these kinds of aneurysms five years ago, there was a real risk of causing some kind of disability for the patient, and the recovery often took weeks. Now, this is almost an outpatient procedure and the results are great."

There are plenty of other advanced imaging strategies that help neurologists and neurosurgeons plan interventions, too. Patients with cranial atherosclerosis – plaque lining the brain's arteries – are at risk of stroke if the plaque becomes so thick that it blocks blood to the brain. "There's a certain threshold of blood flow, or perfusion, that the brain has to have," says Dr. Rasmussen, who is a world leader in endovascular and microsurgical management of aneurysms and other arterial malfunctions in the brain. "If allowed to idle too long, the brain will die." Until recently, there wasn't a good noninvasive way to quantify how much blood was getting to the brain. Now, neurologic specialists can check blood flow through either CT or MR perfusion imaging, which reveals whether a patient is in danger of a stroke even when there are no other signs of danger.

Planning for the removal of brain tumors also has been vastly improved by the 3-D CT models as well as by new advances in MR technology. MR uses a strong magnetic field and radio waves to obtain a chemical analysis of variations in soft tissue that is more detailed than the view yielded by CT. A test called functional MR – fMR for short – tracks the activity of blood in the tissues and can identify functional areas of the brain by identifying which areas have increased blood flow when the patient speaks, moves, looks at a picture, hears sounds, and so on. Neurosurgeons going after tumors don't want to damage any of these functional areas when they operate, so they routinely obtain an fMR before surgery that gives them a map of which areas in the brain to avoid.

Navigating Brain Surgery

Other imaging advances come into play during the actual interventions. For example, some surgery suites now come equipped with Image Guided Surgery (IGS) systems, which operate in the same way that Global Positioning Systems (GPS) help drivers pilot their car from one location to another. First, the patient's head is marked with several beads that will show up during x-ray scanning; then the patient is scanned. After the patient is brought into the operating room, the surgical team touches each of the beads with a special probe. Two cameras mounted on the wall operate like GPS satellites: they triangulate to the probe, and pinpoint the position of the beads relative to the patient's brain.

Movable Imaging A movable MR unit can be used during and after brain tumor surgery to make sure the tumor has been completely removed. "Once you start operating, the older scans aren't necessarily a reliable indicator of what you're operating on," says Gene Barnett, M.D., chairman of the Clinic's Brain Tumor Institute. "The brain floats in fluid and when you open the skull, some of it leaches out and the brain gradually moves. Even removing the tumor itself causes distortion, so this new MR allows us to see exactly what's been taken out and what remains to be done."

Then a computer creates a virtual-reality map of the patient's brain. Wherever the surgeon places the probe, the virtual image not only shows where the probe is – with micro-millimeter precision – but also shows the direction the probe is moving.

This virtual-reality map is then displayed with other information on a workstation screen inside the surgery suite. Since almost all the information from imaging is digital nowadays, surgeons can consult several representations of the patient's brain at once: the virtual-reality map, images from MRs and CTs done days before, as well as a real-time view rendered, depending on the procedure, either by fluoroscopy – a continual flow of x-rays that Dr. Modic likens to shining a flashlight through the body – or endoscopy, created when the probe includes a tiny camera.

Peering Into the Heart

All these advances in the various types of imaging are revolutionizing cardiac care, too. As the overall population ages, it threatens to usher in a corresponding epidemic in heart disease. One of the greatest challenges to cardiac surgeons is helping patients who come with a bundle of health concerns and have already had a number of cardiac interventions. "They present to us with the sum total of all these events," says Richard White, M.D., cardiovascular radiologist. "Now we have to figure out how to get the most out of what's left, which may be limited by the number of veins or arteries that remain available for bypassing."

For these more complicated cases, cardiovascular radiologists also are taking advantage of the new 3-D CT models that allow them to "fly" through coronary arteries and search for abnormalities and the scars and debris from past interventions. They're using MRs to look at the condition of the heart's muscles: to see which are dead or alive and to figure out which will benefit most from an increase in blood flow. The information from these MRs allows them to direct surgeons to the sites of greatest benefit. In addition, the Clinic recently installed a CT system with a PET (positron emission tomography) scanner that allows them to get a better view of each patient's individual coronary artery tree by CT and the condition of the heart muscle by PET. In PET imaging, a radioactive substance is injected into the bloodstream and detectors pick up the energy released as the targeted tissues take up the compound.

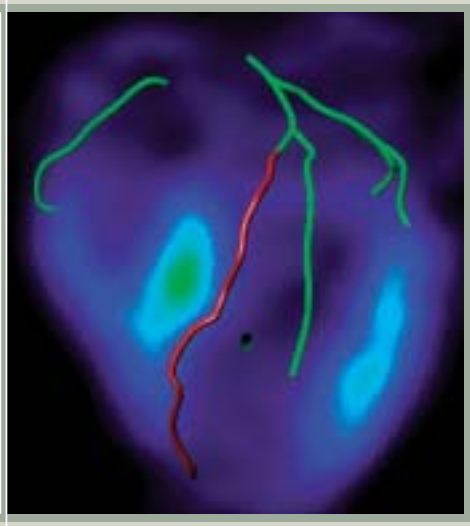
CT helps pinpoint atherosclerosis in the coronary arteries, so it is also helpful for patients at the other end of the disease spectrum: patients who may have problems building up in their coronary tree but are, as yet, unaware of it. As 70 percent of heart attacks occur in the absence of prior symptoms, the new CT approach may help identify people whose only warning signs of heart disease may be family history or an unhealthy lifestyle. "These new kinds of noninvasive imaging help us find patients with sub-clinical disease," Dr. White says. "Patients may be sitting on a time bomb, and the only warning they'll ever have is that first acute event that might be fatal. We can provide them with the kind of information that will convince them that it's time to change their lifestyle or initiate medical therapy."

The Newest View

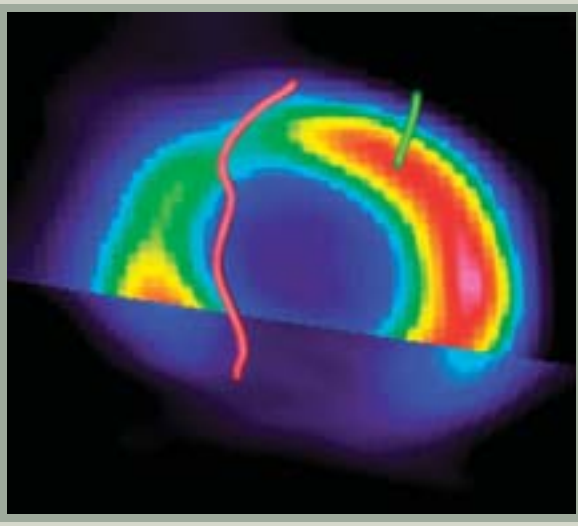
David Huang, M.D., Ph.D., a specialist in cornea and refractive surgery, figured out how to turn some 1990 experiments on corneal thickness using interferometry – a technique using light to make precise determinations of distance – into a new noninvasive, non-contact imaging technology. This technology, called optical coherence tomography (OCT), scans a beam of light across tissue and obtains a very detailed cross-sectional image from beneath the tissue's surface. While this new technology can't probe nearly as deeply into the body as CTs or MRs, OCT delivers extremely high-resolution images that are up to a hundred times more detailed than either of those technologies. It's like viewing the tissue section under a microscope without actually removing or disturbing the tissue.

OCT's high resolution makes it perfect for examining the extremely detailed structures in the eye. "The eye has a clear path all the way to the back," says Dr. Huang. "OCT allows you to see beautiful pictures of structures and layers in the retina – it's the only method that can resolve all these layers."

Since the first commercial OCT became available in 1995, the technology has become a valuable tool for examining macular holes. Another common use is in determining if retinal edema or swelling is causing persistent vision problems following cataract surgery. OCT has also become the most precise way of determining how much damage to the optic nerve and retina nerve fiber layer has occurred in glaucoma patients.



Two different angles of the heart using CT and PET imaging. These images show the association between a closed-off artery (red), decreased blood flow and energy use by the heart. High intensity background colors – red, yellow, green – indicate greater blood flow or greater energy use.



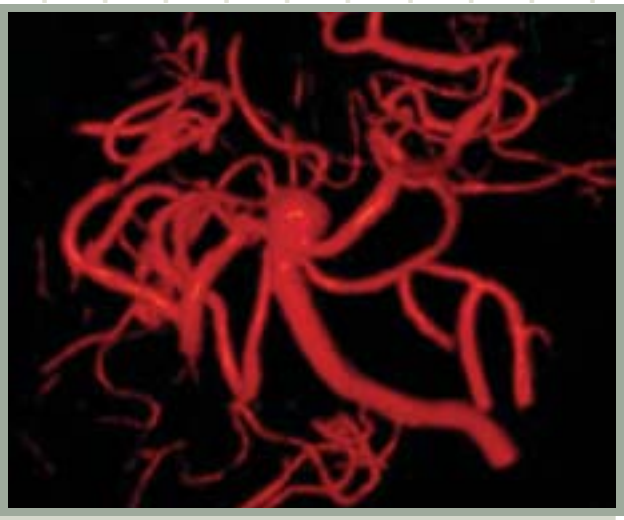
eRadiology Goes the Distance

In their Reading Rooms, Cleveland Clinic radiologists examine all the news – local, national, and international.

Six years ago, the Clinic developed a tele-radiology infrastructure so that radiologists at the main campus could read CTs, MRs and other scans from all over the Cleveland Clinic Health System – from the MR room down the hall to one at the Ashtabula County Medical Center. "After we developed that infrastructure, we realized there was nothing stopping us from reading scans from all over the world," says Michael Recht, M.D., chairman of the Clinic's eRadiology Department. "There's a significant shortage of radiologists and an explosion of imaging technology, so we set about addressing that shortage."

Thus, Cleveland Clinic Star Imaging was born. Through this initiative, Clinic radiologists work with external radiology practices or hospitals to help them build, organize and manage outpatient imaging facilities.

Now that about 80 percent of imaging is digital, it's easier than ever to transmit the results of CTs, MRs and other scans electronically across the Internet. The information is all encrypted for security. This ability makes the Clinic – with its powerhouse of radiology subspecialists – a huge asset to geographically dispersed hospitals and physician groups. "Our radiologists can apply their expertise throughout the country without having to be there," says radiologist David Piraino, M.D.



3D CT angiogram showing a wide-neck aneurysm.

The Cole Eye Institute Staff are involved with a number of studies involving new applications for OCT, too. In one, OCT is being used to map the thickness of the cornea to determine whether or not an individual will be a good candidate for refractive (LASIK) surgery. Another study is checking OCT's ability to determine whether or not people who have already had refractive surgery are good candidates for secondary treatment: OCT allows physicians to look at the internal structure of the cornea and determine if enough tissue is left for LASIK enhancement.

What More Can Imaging Reveal?

Because OCT offers such high resolution imaging, various researchers all over the Clinic are conducting studies to probe new applications for the technology – far from the eye. Dr. Masaryk is one, using a tiny OCT probe attached to the kind of guidewire used for less-invasive surgeries of the brain. Right now, patients who have had an aneurysm sealed off with a coil have to return to the Clinic for biannual or yearly angiograms to check how well the tissues in the arterial walls have healed. The problem is that the angiograms are expensive and only provide indirect evidence of healing. "With the angiogram, you're looking to see if the position of the coil has changed or if a crevice has opened in the tissues – you'd then see dye between the coils," says Dr. Masaryk. "With OCT, the resolution is so great that you can look one time and determine that the tissues have healed. The patient may not need to come back again."

And all over the Clinic, researchers are pushing existing imaging technologies into new areas and using them to answer questions that have long been vexing the medical world. For instance, diagnostic radiologist Micheal Phillips, M.D., is using fMR to probe several mysteries of the brain. In one of the studies, he's using fMR to check the viability of connections between functional areas of the brain in patients with multiple sclerosis, looking to see if there might be some sort of weakness in these connections before a lesion is actually visible. In another study, he's using fMR to evaluate Parkinson's Disease patients who have deep-brain stimulator implants. These stimulators decrease many of the symptoms of this disease and help the patients lead relatively normal lives; however, no one is quite sure why they work. In his study, Dr. Phillips is turning the stimulators off and on, and then using fMR to compare the different patterns of blood flow in an effort to understand how the stimulators work – and maybe even get some ideas how they might be made more effective.

"Metallic objects like the stimulators can heat up in a MR scan and present a danger to the patient," Dr. Phillips says. "The Clinic is the only place where we've done the appropriate safety work to eliminate this risk. In our study, the heating does not occur and the brain is safe." ■

To see more images including a rotating, beating heart, go to:
www.clevelandclinic.org/clevelandclinicmagazine

Isador Lieberman, M.D.,

FROM VISION TO INVENTION:

BRINGING MEDICAL INNOVATIONS TO PATIENT CARE

Merlot Bone Anchor

"Biomedical innovation in our nation over the past half-century equals or exceeds the value of innovation from all other sectors of the American economy combined.... Despite the tremendous progress of recent decades, most medical experts will agree that the most important medical innovation is probably still ahead of us."

Mark McClellan, M.D., Ph.D.
Commissioner of the U.S. Food and Drug Administration
Speaking at the Cleveland Clinic Medical Innovation Summit
October 2003

After a full day of orthopaedic and spinal surgery, Isador Lieberman, M.D., headed to his lab to continue working on a problem he'd been struggling with for four years.

He wanted to find a way to fix scoliosis – or curvature of the spine – endoscopically. In other words, instead of using the traditional method of exposing the patient's entire spine with a large incision through the chest, he would make small holes. That would allow the patient to heal much faster.

But the problem was that the rods used to fuse bones and straighten the spine had to be attached with screws and nuts that look a lot like those pieces you'd pick up at your local hardware store. The rod would slip as the patient moved if it wasn't secured with a nut on the other side.

But no matter what Dr. Lieberman tried, he couldn't get all the pieces and parts assembled easily and consistently through the small holes.

He says it was like building a ship inside a bottle or – worse yet – "like those kid mazes with the little balls that you have to get in the holes."

By 2 a.m. he confesses to using a few stronger words and deciding, flat out, that it was over. He would walk away from four years of research.

By the time he got home, he was exhausted and depressed. He got out a bottle of wine, figuring that at least a glass would end the day on a better note and ease his way to sleep.

And that's when it hit him. It was like the moment in a classic cartoon when a light bulb appears over the character's head.

"As I uncorked the bottle of wine, I realized 'This is it! This is what I need to make my implant work!'"

The next day he returned to his lab with his corkscrew in hand. He screwed it into a piece of bone and realized he couldn't pull it out. Even without a nut securing it on the other side, that corkscrew stayed in the bone, no matter how he moved and pulled on it.

Today, that same corkscrew sits in his Clinic office as a reminder of the moment that changed everything.

That was the birth of the Merlot Bone Anchor.

But, it was only the beginning. Dozens of prototypes, eight patents and eight years later, the Merlot Bone Anchor – which now features a double helix design (like two parallel corkscrews) – still isn't on the market.

"Every day in the operating room, I wish I had the Merlot Anchor right now," Dr. Lieberman says. "But it's understandable – we've got to prove these things. We've got to do it right."

A History of Innovation

Dr. Lieberman's invention – like hundreds of others each year – is being helped down the commercialization path by CCF Innovations (CCFI). Founded in 2000, this internal group is dedicated to commercializing Clinic technology and bringing it to market through spin-offs, equity partnerships and licenses.

"The idea underlying CCFI is that physicians and researchers here are in a good position to identify needs that we can meet with new technology or techniques," says Joseph Hahn, M.D., chairman of CCFI. "If, in creating this technology, we're going to have better patient care and the device or procedure is going to be cost-effective, then that's the kind of invention we can work to commercialize."

Although CCFI is a youngster at just four years old, the history of what used to be called "tech transfer" at The Cleveland Clinic is a long one.

Archives show that as early as 1906 Clinic founder George W. Crile, Sr., M.D., working with George Ketteringham, produced the equipment used for the first successful human-to-human blood transfer. When The Cleveland Clinic opened in 1921, Dr. Crile employed a toolmaker and a glassblower to make new medical devices.

The first record of commercialization of a device is in 1930 when Clinic physician Maria Telkes, M.D., patented and marketed her "electro-osmotic generator." What exactly that did has been lost over the years, but it is thought to have been used in experiments on the conduction of electricity in living tissue.

While it was fairly common to patent and commercialize medical devices, other inventions such as surgical procedures were often just shared between physicians.

One of the Clinic's most historical achievements – bypass surgery – was never officially patented or commercialized, yet hundreds of thousand of patients have benefited since its conception in 1967.

Aaron Fleischman, Ph.D. and Shuvo Roy, Ph.D.

MAKING IT SMALL

Shuvo Roy, Ph.D., always assumed that some day he'd work for NASA or a private aerospace company. After all, with an electrical engineering doctorate from Case, where he worked on ice detection systems for airplane wings and high temperature flow sensors for jet turbine engines, what job could be more perfect?

But all that changed when he got a call from fellow graduate student Aaron Fleischman, Ph.D. Fleischman – also graduating with his doctorate in engineering from Case – had just returned from an interview at The Cleveland Clinic and told Roy that he should interview there, too.

The rest, as the cliché goes, is history.

In 1998, Drs. Fleischman and Roy teamed up to open the BioMEMS Laboratory in the Department of Biomedical Engineering at the Clinic's Lerner Research Institute.

They are among 25 principal investigators in Biomedical Engineering, the largest research department at Lerner and one of the key centers of innovation at the Clinic.

MEMS stands for Micro-Electro-Mechanical Systems. One common use for MEMS technology is a car's airbag sensor, the tiny device that registers the impact of an accident and signals the airbag to release. Another everyday MEMS device is the nozzle on an inkjet printer. There's a heat sensor in a silicon chip that, when heated, signals ink to shoot onto the page.

Dr. Roy says another way to think of MEMS is "electronics plus something else." That "something else" is usually a mechanical device.

MEMS devices are extremely tiny, measured in micrometers or 1/10,000ths of an inch. One tiny MEMS chip can hold a complex laboratory of information within it. They are made from silicon because they can be integrated with microprocessors and electronic and computer chips via batch manufacturing, keeping costs low and allowing for precise reproduction of thousands of devices at one time.

BioMEMS, then, is the biomedical application of such a device. One of Dr. Roy's first projects was to translate his

(Continued on page 20)

A New World

In 1980, the world of medical innovation changed with the passage of the Bayh-Dole Act. That statute allowed academic centers to maintain ownership of inventions supported by federal funds. Since many clinicians and researchers receive financial support from the National Institutes of Health, the Bayh-Dole Act gave individual inventors a new financial incentive to create. However, most physician-inventors say it's not the money that motivates them.

"For me, the motivator is my patients, to do something better for them, to contribute to spine surgery," Dr. Lieberman says.

Once an idea is in motion, physicians and researchers describe the process of bringing inventions to market as inspirational and, sometimes, frustrating. Along the way, there are dozens of questions that must be answered to make sure the innovation – a device, medication, diagnostic test, or procedure – is even worth commercializing.

"Any time you get a new invention, one that's viable, you have the question: Can you get additional resources to drive it to the next level?" says Chris Coburn, executive director of CCFI. "Those resources might be venture capital. It might be government grants. It might be internal funds. And then, ultimately, can you get regulatory approval and will insurers reimburse?"

The process to bring an idea to market starts with expensive research and studies. Then it must receive Food and Drug Administration (FDA) approval – something that can take months or years, depending on whether the product is an offshoot of a previously approved product or something altogether new. Finally, the new product, drug or procedure must be insurance-reimbursable as determined by the Centers for Medicare and Medicaid Services (CMS).

Creativity in Their Blood

Coburn says that more than half of all Clinic inventions come from physicians who developed them out of a need they've seen in their practice, such as Dr. Lieberman's Merlot Bone Anchor.

Delos "Toby" Cosgrove, M.D., chairman of the Clinic's department of Thoracic and Cardiovascular Surgery, is one of the world's top inventors of devices for cardiac surgery. He holds 19 patents, many resulting in products including some that bear his name. The most famous is the Cosgrove-Edwards Annuloplasty Ring used to reinforce valve repair. In his 30s, Dr. Cosgrove discovered that he has dyslexia, a learning disability. He attributes much of his creativity to the dyslexia that allows him to "think differently than other people do."

Cosgrove-Edwards Annuloplasty Ring

Dr. Lieberman says that spinal surgery was a perfect fit for him as the son of a carpenter and a seamstress. As a child, he was always building go-carts and tree forts or tinkering with electronics. Today, even when he's not in the lab or the operating room, he's often thinking of his next invention. He keeps a notepad next to his bed. He says it's not unusual for him to wake up at 2 a.m. and draw out a diagram of a new device.

Image, center: Top-down view of a coronary artery using Virtual Histology Intravascular Ultrasound (IVUS). Colors indicate: dark green is fibrous tissue, light green is fibrous tissue that is starting to accumulate cholesterol, red is cholesterol-induced dying tissue and white is calcium. Red and white parts are of particular concern in diagnosing coronary artery disease.

Thinking constantly about what to invent next is a common thread Dr. Lieberman says he has seen in other physician-inventors.

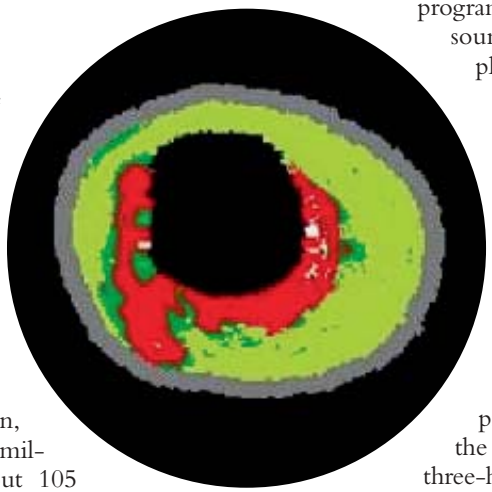
"We look at something and ask 'Why is that designed that way? Why is that made that way? It's wrong. It doesn't work that way. It's more of an analytic mind when you look at something. We have whatever it is in our background, our DNA, our genes that triggers that thought process."

Double-time for Research

Last year, CCFI reports, the Clinic had more inventions and filed more patent applications per dollar of research than the Mayo Clinic in Rochester, Minnesota; Johns Hopkins Medical Center in Baltimore and Massachusetts General Hospital in Boston.

In 2003, the Clinic performed more than $100 million in "sponsored" research, that is research paid for by the government, corporations or foundations, and had 112 new inventions. In comparison, Ohio State University spends about $400 million in sponsored research and had about 105 inventions in the same time.

The Clinic employs more than a thousand researchers – from principal investigators to graduate students – at its Lerner Research Institute. But with the growth in commercialization, many of those dedicated researchers also end up splitting their time – or as they say, doubling their time – working on new ventures.



For example, Geoffrey Vince, Ph.D., a biomedical engineer at the Lerner Research Institute, works as a full-time researcher for the Clinic, as well as a consultant for Volcano Therapeutics based in Rancho Cordova, California.

Volcano licensed Dr. Vince's innovation, called Virtual Histology Intravascular Ultrasound (IVUS), a software program that uses radio frequencies from an ultrasound probe to color-code the different types of plaque inside a coronary artery.

This technology can alert a physician to critical "vulnerable" plaque that can cause a deadly heart attack in an instant, even when the plaque is too small to block an artery. In fact, Dr. Vince says two-thirds of the plaques that kill people are in arteries that are less than 50 percent blocked.

CCFI negotiated the license with Volcano, as well as Dr. Vince's role with the company. He spends time working with Volcano's engineers to further develop the product and trains the company's sales reps on the product they're marketing. Dr. Vince says the three-hour time difference between Cleveland and California helps, so that he can work as a consultant long into the evening.

Clinic researchers must be cleared through a conflict-of-interest committee before being permitted to work as a consultant to an outside company. The arrangement adds to the Clinic's prestige and ultimately benefits the Clinic financially. The Cleveland Clinic name will appear on the Virtual Histology software that Volcano sells.

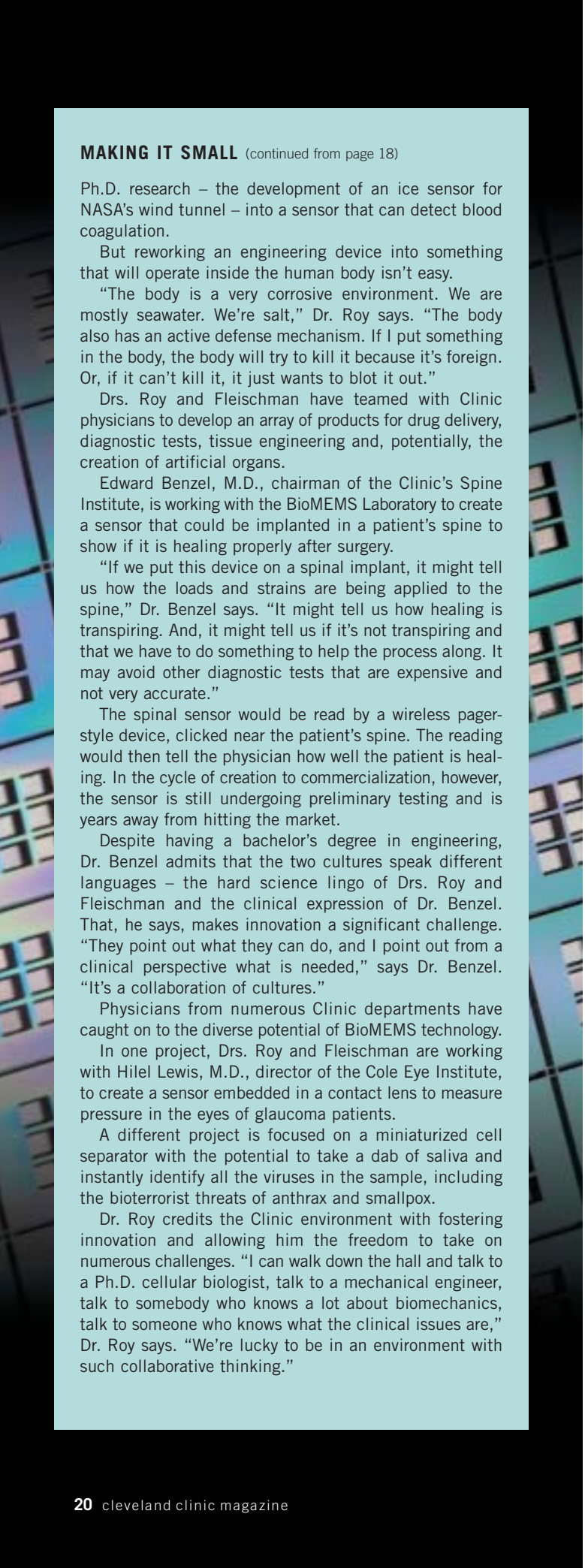
Chris Coburn and Joseph Hahn, M.D.

INVESTING IN INVENTING

WHILE THE COST OF INNOVATION CAN BE STAGGERING, THE POTENTIAL GAIN IS STUNNING AS WELL.

- Cost of development of a single medical device: Approximately $100 million [1]
- Total medical device market size: More than $55 billion [1]
- Development cost of a new drug: More than $800 million [2]
- Size of U.S. pharmaceutical market (2001): More than $175 billion [3]
- In 2000, there were an estimated 7,000 new pharmaceuticals in development in the U.S.[1]

[1] *Venture Reporter* magazine
[2] *Tufts University Research Study*
[3] *National Institute for Health Care Management*



MAKING IT SMALL (continued from page 18)

Ph.D. research – the development of an ice sensor for NASA's wind tunnel – into a sensor that can detect blood coagulation.

But reworking an engineering device into something that will operate inside the human body isn't easy.

"The body is a very corrosive environment. We are mostly seawater. We're salt," Dr. Roy says. "The body also has an active defense mechanism. If I put something in the body, the body will try to kill it because it's foreign. Or, if it can't kill it, it just wants to blot it out."

Drs. Roy and Fleischman have teamed with Clinic physicians to develop an array of products for drug delivery, diagnostic tests, tissue engineering and, potentially, the creation of artificial organs.

Edward Benzel, M.D., chairman of the Clinic's Spine Institute, is working with the BioMEMS Laboratory to create a sensor that could be implanted in a patient's spine to show if it is healing properly after surgery.

"If we put this device on a spinal implant, it might tell us how the loads and strains are being applied to the spine," Dr. Benzel says. "It might tell us how healing is transpiring. And, it might tell us if it's not transpiring and that we have to do something to help the process along. It may avoid other diagnostic tests that are expensive and not very accurate."

The spinal sensor would be read by a wireless pager-style device, clicked near the patient's spine. The reading would then tell the physician how well the patient is healing. In the cycle of creation to commercialization, however, the sensor is still undergoing preliminary testing and is years away from hitting the market.

Despite having a bachelor's degree in engineering, Dr. Benzel admits that the two cultures speak different languages – the hard science lingo of Drs. Roy and Fleischman and the clinical expression of Dr. Benzel. That, he says, makes innovation a significant challenge. "They point out what they can do, and I point out from a clinical perspective what is needed," says Dr. Benzel. "It's a collaboration of cultures."

Physicians from numerous Clinic departments have caught on to the diverse potential of BioMEMS technology.

In one project, Drs. Roy and Fleischman are working with Hilel Lewis, M.D., director of the Cole Eye Institute, to create a sensor embedded in a contact lens to measure pressure in the eyes of glaucoma patients.

A different project is focused on a miniaturized cell separator with the potential to take a dab of saliva and instantly identify all the viruses in the sample, including the bioterrorist threats of anthrax and smallpox.

Dr. Roy credits the Clinic environment with fostering innovation and allowing him the freedom to take on numerous challenges. "I can walk down the hall and talk to a Ph.D. cellular biologist, talk to a mechanical engineer, talk to somebody who knows a lot about biomechanics, talk to someone who knows what the clinical issues are," Dr. Roy says. "We're lucky to be in an environment with such collaborative thinking."

Spin-Offs vs. Licenses

Coburn says CCFI's ultimate goal is to "ring the campus with many, many companies." But, despite a wealth of ideas, that's not an easy job. Coburn says as few as 20 percent of the inventions that come into a technology commercialization office ever get off the ground.

"We end up seeing a lot of ideas that are wonderful. But once we get into evaluating them, either they're not addressing a market problem, or they're not addressing a clinical need, or the number of patients is so small that it would be prohibitively expensive to move forward with it," says Dr. Hahn.

Once an invention makes it through the hurdles of FDA approval and CMS reimbursement, the next job for CCFI is to determine how to handle it in the marketplace. Should the Clinic start a new spin-off company or should it license the technology to an experienced, existing company?

"The depth and breadth of the portfolio are key," says Dr. Hahn. "If it's just one invention – unless it's a real blockbuster – that may be difficult to start a company around. On the other hand, if it's several inventions, several patents, several ideas, it gives a lot more credence to the idea that maybe we've got something here."

Since its inception, CCFI has spun off or partnered with 16 companies. In 2003, CCFI started three companies and entered agreements for 20 licenses. Spin-off companies run the gamut of medical specialties. They include CleveX, which has a device for removing skin lesions; Ridgeway, a cancer therapeutic company; PeriTec, which uses peritoneal tissue to line stents, grafts and patches; and Cleveland BioLabs, whose technology increases tolerance to chemo and radiation treatment.

CCFI announced one of its most recent spin-offs, PrognostiX, in January of this year. In addition to Clinic support, the Arkansas-based company ExOxEmis has invested $6 million in PrognostiX.

PrognostiX is based on the research of Stanley Hazen, M.D., Ph.D., who heads Preventive Cardiology and Cardiac Rehabilitation. The new company is focused on using chemical approaches to identify biomarkers that serve as "molecular fingerprints." These markers will be useful in creating diagnostic or prognostic blood tests for various inflammatory diseases, including atherosclerosis and asthma.

"You cannot launch a company unless the inventor wants it badly enough, because it's a lot of work and a lot of risk," adds Coburn. "How badly does the inventor want it? Does his or her family support it? You can't be a casual entrepreneur."

Just ask Dr. Lieberman about how much he wants it.

He's been working on an endoscopic spine surgery procedure since 1992 and the Merlot Bone Anchor since 1997. In the meantime, he also has seven other patents pending for everything from artificial disks to bone-cutting tools. His vision is that one day his inventions will be in orthopaedic operating rooms worldwide.

"Development work is inspiring," he says. "This becomes like your child. When something doesn't work, you cry. You're upset. When something does work, you're very proud." ■

MEDICAL DEVICE INNOVATIONS: WHERE POSSIBILITIES BECOME PROTOTYPES

Two large pieces of metal lie on the floor of what looks like a mini-factory in the Cleveland Clinic's Lerner Research Institute.

The whirring machinery here stamps out prototypes of medical devices imagined by clinicians and researchers to help with diagnostic testing or surgical procedures. But it's tough to imagine how these huge metal blocks could be used in an operating room or diagnostic testing center.

And, in fact, they won't be. The shiny silver platforms will be foot rests for an ingenious new virtual treadmill that may one day be used on the International Space Station. As the astronaut watches a video of different environments – uneven ground, running the Boston Marathon or climbing stairs – the footholds move as a leg would move on that terrain.

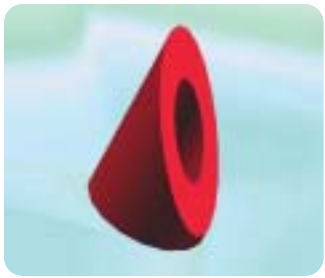
Elsewhere in the building, a group of engineers is putting together an electronic battery pack that they hope will reach the moon some day. This one is designed to monitor the muscle movements of astronauts, who can suffer from bone loss and muscle atrophy in space.

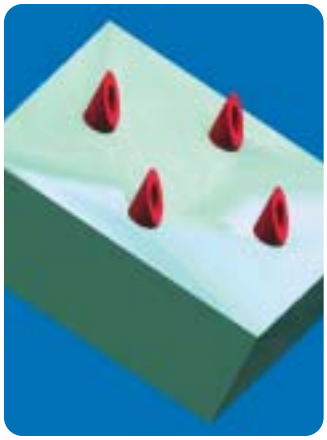
And, down the hall, there's a room with a human-size artificial heart made out of metal that researchers hope will extend life someday for those waiting for a transplant, or maybe even replace transplants all together.

From space devices to out-of-this-world concepts like an implantable total artificial heart, these are some of the projects advanced by the Clinic's Medical Device Innovations (MDI) program. MDI is a part of Biomedical Engineering and most of the people who work here are engineers or technicians, not physicians.

Within MDI are four subgroups: Mechanical Prototype Core, Polymer Laboratory, Engineering Design and Electronics. The Clinic is one of only a handful of health centers worldwide to offer those disciplines on the same campus as its clinicians and researchers.

The initial ideas come from physicians or researchers who at some point – maybe during surgery or assessing a patient or reviewing research data – think, "If only I had…"





CAD prototype drawings, like this one of silicon micro-needle tips, help innovators visualize their ideas, working out potential design problems before a physical prototype is produced.

Tony Shawan, manager of MDI's Mechanical Prototype Core, says his group often makes trips to the operating room to see firsthand what the physician has in mind. They've worked off everything from a design roughly sketched out on a napkin to formal computer drawings.

"While it takes a long time to get a new medical device to market, it takes the MDI group just a few months, on average, to develop a prototype to demonstrate the new technology," says Peter Cavanagh, P.h.D., chairman of Biomedical Engineering. The four labs in the MDI group work with all clinical disciplines, including cardiothoracic, orthopaedics, neurology and urology.

"First we talk with the inventor to really understand the idea, to understand its technical complexity," Mark Goodin, manager of MDI, says. "Then we ask, 'What is needed to convey the idea?' Sometimes it's just a three-dimensional CAD [Computer-Aided Design] model. We can also take it to another level and demonstrate how the invention works by building a physical prototype."

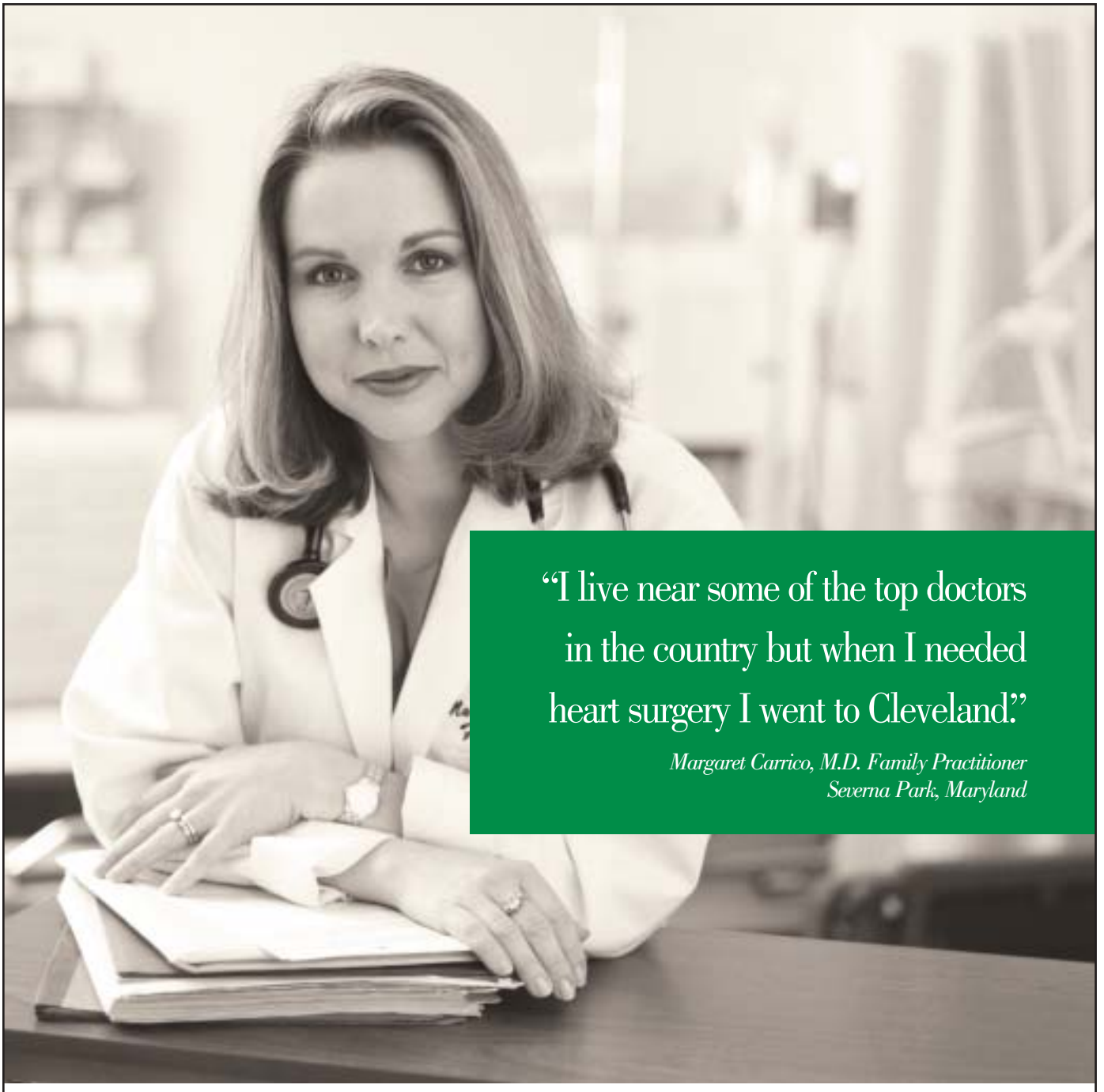
The MDI labs that make those prototypes are packed with unique computer programs and machinery. One computer technique – called Computational Fluid Dynamics – can demonstrate flow patterns through or around a device, ideal for the design of catheters used to deliver drugs.

Another approach – called Stereo-lithography – builds solid models out of liquid polymer, curing one thin layer at a time. That machine can even import a patient's CT scan and MR image and within a day will replicate the image in plastic. That is ideal in dentistry. The machine simply converts the CT data and makes a plastic model of the patient's jaw, allowing the doctor to know the exact jaw depth for implants.

MDI's motto is "Every Good Idea Deserves A Chance." But Ji-Feng Chen, a principal research engineer in the Polymer Lab who has helped to develop the artificial heart, sums it up best when he says, "We make dreams come true."

And if that means reaching for the moon, the MDI engineers won't hesitate to do it.

For more on MDI and innovation, go to www.clevelandclinic.org/clevelandclinicmagazine



Over 100 doctors select The Cleveland Clinic for their heart surgery every year.

For more information on the heart center rated #1 in the nation by *U.S.News & World Report,* or to schedule an appointment, call toll-free at 866/289-6911. Or visit us at: www.clevelandclinic.org/heartcenter.

THE CLEVELAND CLINIC
Heart Center
Every Life Deserves World Class Care

FUTUREHEART

TODAY CARDIOVASCULAR DISEASE AFFECTS MORE THAN 65 MILLION PEOPLE IN THE UNITED STATES.

BY 2015 AN ADDITIONAL TEN MILLION AMERICANS WILL BE OVER THE AGE OF 65, BRINGING WITH THEM ALL THE HEART CARE CONCERNS THAT COME WITH AGE. WILL OUR HEALTHCARE SYSTEM BE READY? HERE'S HOW THE NATION'S #1 HEART CENTER PROVIDES STATE-OF-THE-ART HEART CARE TODAY WHILE PREPARING FOR THE CARDIAC CARE WE'LL NEED TOMORROW.

Last summer, in a hospital in Venezuela, Cleveland Clinic cardiologist Patrick Whitlow, M.D., made medical history. That day Dr. Whitlow, along with Clinic echocardiographic expert Leonardo Rodriguex, M.D., and Venezuelan cardiologist José Condado, M.D., repaired the leaking mitral valve of a patient's heart without surgery or opening the chest.

No cutting, no blood, no need for a lengthy recovery.

Although it sounds like science fiction, Dr. Whitlow and a cardiology team repeated the feat at The Cleveland Clinic a few months later.

The patient was a man from Youngstown, Ohio, who agreed to forego the proven, traditional mitral valve surgical repair for this ground-breaking procedure.

Dr. Whitlow says the hope is that this procedure will help save the lives of people whose health is too fragile to undergo surgery since it doesn't put the kind of strain on a weak heart that traditional surgery does.

Toby Cosgrove, M.D. (left) and Eric Topol, M.D., co-chairmen of the Heart Center, with a preliminary model of the new Heart Center.

In this procedure, the catheter is threaded through the leg to the heart, much like with an angioplasty.

"But that's where the similarity ends," Dr. Whitlow explains. "We go in the vein instead of the artery. The vein is a structure that can accept very large catheters without causing a problem."

The procedure involves guiding the catheter through the femoral vein in the thigh up to the right side of the heart. Then the physician crosses the catheter over the atrial septum into the left side of the heart. While watching on an echocardiography machine, the physician can see where he needs to place a clip over the leak in the mitral valve.

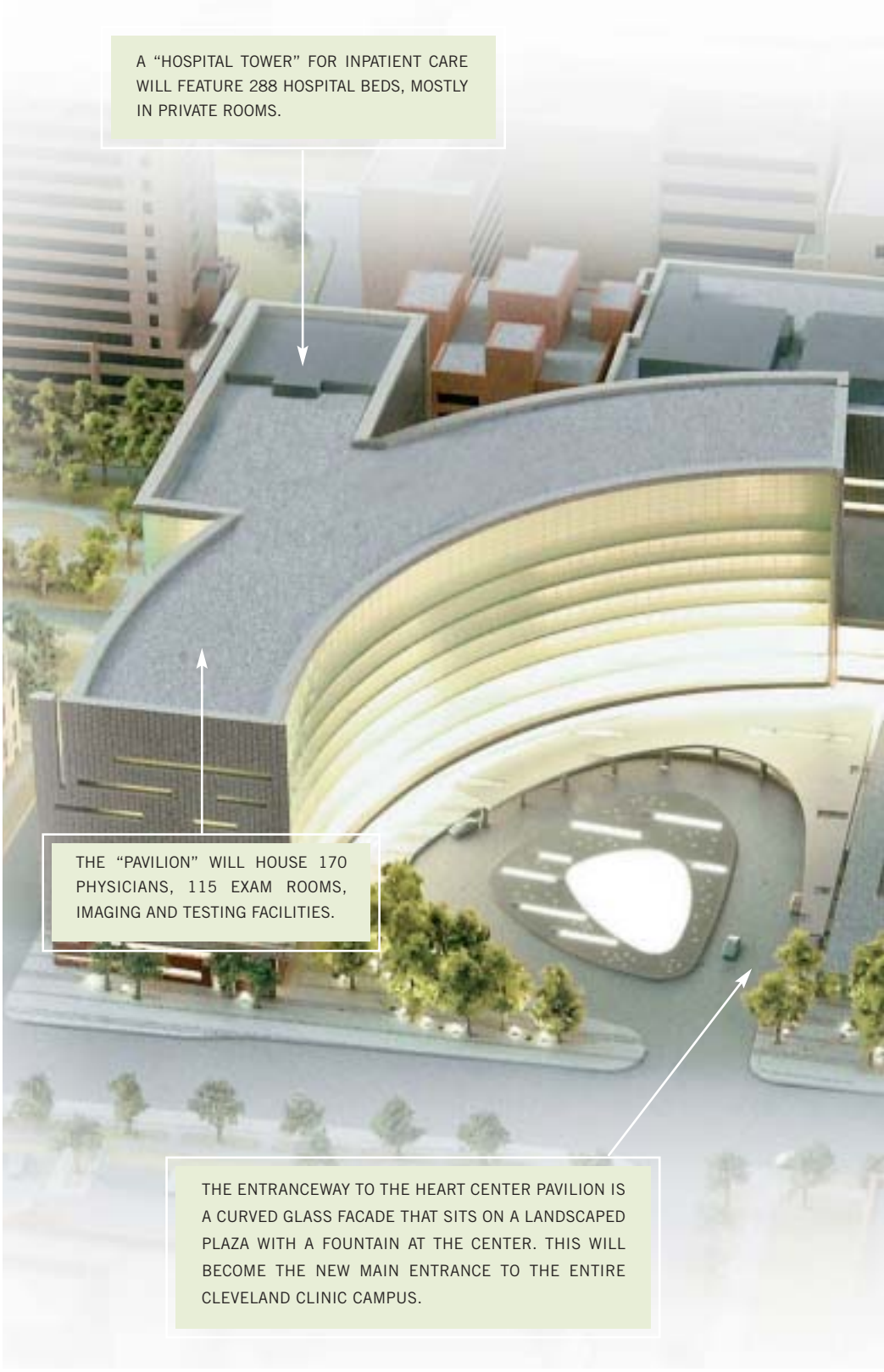
A California-based company called Evalve spent three years developing the clip and contacted Dr. Whitlow about finding the best way to use it in patients. Catheter crossover has been used for other heart repair procedures, but never for a leaking mitral valve. A Phase I study is currently under way at five medical centers, including the Clinic. This study will determine if the procedure is feasible and safe for selected patients who otherwise would be candidates for surgery.

THE BEST

That study is just one of many cardiology research studies currently taking place at the Cleveland Clinic Heart Center, named America's best heart center by *U.S. News & World Report* for ten years straight.

The Clinic, in fact, has a rich history of innovation. (See timeline below.) Clinic physicians have pioneered such revolutionary procedures as coronary angiography, coronary bypass surgery, aortic valve repair, carotid artery stenting and curative treatment of atrial fibrillation.

Last year, Clinic physicians rocked the cardiology world with research targeted at eradicating heart disease, including the discovery of the first heart disease gene, as well as ways to actively dissolve plaque buildup inside artery walls.



1956

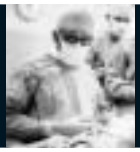
WORLD'S FIRST STOPPED-HEART SURGERY PERFORMED

1958

WORLD'S FIRST CORONARY ANGIOGRAM PERFORMED

1967

CORONARY BYPASS SURGERY PIONEERED



THE "TECHNOLOGY BUILDING" WILL FEATURE LEADING-EDGE TECHNOLOGY USED FOR CARDIAC SURGERY AND PROCEDURES, SUCH AS CARDIAC CATHETERIZATIONS.

THE BUILDING

THE NEW HEART CENTER WILL BE A 950,000 SQUARE FOOT CENTERPIECE TO THE CLINIC MAIN CAMPUS THAT WILL BE BUILT ALONG EUCLID AVENUE AND E. 96TH STREET.

A NEW PARKING GARAGE ACROSS EUCLID AVENUE WILL HAVE AN UNDERGROUND CONCOURSE LEADING TO THE PAVILION.

THE NEED

Success has not come without growing pains. The world's best heart center also is one of the world's busiest with more than 88,000 patients seen annually. Today, the cardiology department is literally bursting at the seams.

"We've been growing exponentially," says Eric Topol, M.D., the Clinic's chairman of Cardiovascular Medicine. "I got here in 1991 and over that time, we have five-fold as many patients and procedures. At the moment, we're making the most of what we have."

"We've outgrown our physical facilities," says Delos "Toby" Cosgrove, M.D., chairman of the Clinic's Thoracic and Cardiovascular Surgery. "Patients are everywhere, in all the existing usable space. We need space."

The current packed facilities – along with rapidly changing procedures used to treat heart disease – is why the Clinic has launched a $300 million campaign to build a new heart center.

"The way things are done today is very different than a decade ago," Dr. Topol says. "Tests, like imaging – whether it's echo or nuclear test or electrical – were not as instrumental or vital back in the early '90s. Now they are part and parcel of every comprehensive evaluation."

Dr. Topol says that, in addition, the need and types of cardiac surgery have changed, while procedures such as stenting have increased. Catheter treatment or surgery to cure atrial fibrillation, a rhythm problem, is now commonplace.

New innovations – consider the example of Dr. Whitlow's valve repair without surgery – are coming about every day within the Clinic.

"I think part of the reason the Clinic is where it is in 2004 is because we aren't satisfied with the way patients are being treated today," says Dr. Whitlow. "We're always doing things to make the options better."

One of the biggest changes in cardiology has been in the management of heart failure. Transplantation used to be the only option available when the heart muscle began to wear out.

The Cleveland Clinic did its first transplant in 1984. The man who received the second transplant is still alive, nearly 20 years later. In 1998, the Clinic did 113 transplants in one year – a record held to this day.

High-tech imaging suite

Today, with more than 1,000 transplants under its belt, the Clinic has the nation's third largest transplant program. It performs almost 70 percent of all transplants in Ohio. Still, transplants are hard to come by because there aren't enough donor organs each year to save the lives of everyone who needs a transplant.

It's the innovation behind finding ways for heart failure patients to live longer and with a better quality of life through procedures other than transplants that is the strength of the Clinic's Heart Center, says Nicholas Smedira, M.D., director of Cardiac Transplantation and Ventricular-Assist Device Therapies.

Repairing valves, reshaping the heart or adding mechanical devices for electrical conduction are all options now available to patients who need a transplant, allowing them to extend their lives while they await an appropriate organ. The Clinic is one of the world's leading facilities in treating heart failure through team collaboration, rather than just waiting for a transplant.

"The new Heart Center will allow this type of intense, interdepartmental collaboration to continue to find the best ways to treat patients with advanced heart failure," says Dr. Smedira. "A team, a group of specialists, treating each patient is going to have a better impact

1976

AMERICA'S FIRST DEPARTMENT OF CARDIOTHORACIC ANESTHESIOLOGY FOUNDED

1986

CARDIOTOMY AUTOTRANSFUSION, USING PATIENT'S OWN BLOOD FOR TRANSFUSION, DEVELOPED

1991

AORTIC VALVULOPLASTY, FOR REPAIRING RATHER THAN REPLACING DISEASED VALVES, PIONEERED

Operating room

on that patient's health. That's what the new Heart Center will help us provide."

Take preventive cardiology. In recent years this specialty has moved to the medical care forefront, utilizing a multidisciplinary approach for assessment and treatment of patients who have significant risk factors for heart disease. Physicians with specialty training in cardiology, endocrinology/diabetes/metabolism, renal/hypertension, heart failure, cardiac imaging, internal medicine and women's health offer preventive cardiovascular medical care.

Today, Preventive Cardiology and Cardiac Rehabilitation is located away from the main cardiology area. The new Heart Center will better integrate this section.

THE CAMPAIGN

The Heart Center campaign began quietly in early 2003 with solicitation to major philanthropists and Clinic supporters. By late in the year, the Clinic had pledges from more than 10,000 individual donors, along with corporations and foundations, for a commitment of about $147 million – just about halfway to the $300 million goal. While about half of the donations have come from within Ohio, the remaining 50 percent have come from the other 49 states and seven foreign countries.

Now in the midst of a vocal, public campaign, the Clinic needs to know the rest of the dollars are on the way before construction will begin.

So far, individual contributions have ranged from $25 to $11 million, says August Napoli, vice chairman for the division of Institutional Relations and Development. Napoli says that all donations – no matter how big or small – are needed and appreciated. "Heart disease matters to everyone," he says.

In fact, heart disease is America's number-one killer, taking a life every 33 seconds. One little-known fact is that heart disease kills more women over the age of 65 than all types of cancers combined, including breast cancer.

Although the disease impacts the lives of so many, getting the general public to understand the need to contribute to a new Heart Center can still be a tough sell, says Napoli.

"Philanthropy and medical centers don't have a long history with each other because there used to be a large profit margin in medicine," he explains.

That changed, however, with insurance companies and managed care.

Now, medical centers that want to grow usually must do so with contributions from individuals, corporations, foundations and government grants. Today, hospital fundraising campaigns must function more like an academic environment, rather than a corporation, to be successful.

Colleges and universities typically have used a fundraising campaign structure called "chapters" and that's exactly how the Cleveland Clinic Heart Center campaign has been set up. Most people are familiar with alumni chapters that generate funds for a university. The Clinic is using that same philosophy with chapters in 13 cities in the United States and three countries where potential donors and dedicated volunteers reside. Another 20 potential cities have been pinpointed as sites for possible chapters.

THE IMPACT

Of course, the city where most of the donations have come from so far – and are expected to continue – is Cleveland. The new Heart Center will generate jobs, fuel the economy and impact the city and state with tax revenues.

"Medicine and healthcare is the new steel industry," says Napoli. In fact, the statistics are startling.

"The proposed Heart Center at The Cleveland Clinic not only represents 1,500 new jobs and annual income taxes in excess of $9 million, it further positions

Cardiovascular ICU

the Clinic as the top cardiac care facility in the world," Cleveland Mayor Jane Campbell told *Cleveland Clinic Magazine*. "All told, this project will yield a $1 billion economic impact on our region. The City of Cleveland is pleased to support this project and is working with the Clinic on infrastructure needs as well as advocacy for federal and state funds."

Ohio Governor Bob Taft says that he is excited about the potential for the new Heart Center.

"This new center will provide leading advanced technology, research and patient care in the fight against heart disease, new high-paying jobs, and will further promote

1992

FIRST HOSPITAL TO VOLUNTARILY RELEASE OUTCOMES DATA AND MORTALITY STATISTICS TO THE PUBLIC

1996

WORLD'S FIRST MINIMALLY INVASIVE HEART VALVE SURGERY PERFORMED

the Clinic's tradition of providing world-class healthcare," Taft says. "Projects like this support the Third Frontier Project's core goals – making Ohio a leader in advanced technology and research, creating jobs and improving the quality of health for all Ohioans."

THE GOAL

Some of those new jobs will be for physicians and researchers. The leading cardiologists currently at the Clinic see a new Heart Center as a strong and necessary recruiting tool to continue to bring the best and brightest people to the Clinic.

"To continue to attract quality people, we need to have a first-class physical facility to house them," says Dr. Cosgrove.

Dr. Cosgrove says the Clinic has entered a partnership with Royal Phillips Electronics to use and help develop the latest technology. But more important than the technology are the physicians who use it for the benefit of patients. Physicians such as those in Dr. Smedira's group who are finding innovative ways to replace heart transplants. Or those on Dr. Whitlow's team who are researching nonsurgical procedures for valve repair. Or those conducting advanced scientific research into genetics or stem cells to repair the heart.

Supporters of the new Heart Center agree that it's not just about building a glorious new structure to help beautify the city of Cleveland. It's about generating jobs, empowering innovation, attracting talent, and helping the average patient.

It's about conquering heart disease altogether. ■

To learn more about the new Heart Center, go to www.clevelandclinic.org/clevelandclinicmagazine

THE HOUSE THAT HEART CARE BUILT

Henry Chao is modest about his role as one of the lead architects of the proposed new Cleveland Clinic Heart Center. Instead, he credits the Cleveland Clinic physicians with having a clear vision of where they want to work. His job, he says, was simply to make it happen.

Members of NBBJ, located in Columbus, Ohio, first met Cleveland Clinic Chairman and CEO Floyd D. Loop, M.D., halfway across the world in Turkey. NBBJ – which specializes in designing healthcare facilities – was working on a large healthcare, hotel and entertainment complex in Istanbul. After the success of the design for the Istanbul project, Dr. Loop invited NBBJ to present design options for the new Heart Center.

Chao says what first hit him was the magnitude of the project – 950,000 square feet, making it the largest single purpose medical facility in the world. Despite the size, he knew he wanted to design a place that was warm and personal. So, before creating designs, the NBBJ team took the time to get to know the Clinic campus, as well as the surrounding Cleveland neighborhood.

"We designed this with the doctors," Chao says. "We have gone through rounds and rounds of meetings for not only what they needed, but what they preferred for the environment." That alone, Chao confesses, was a bit intimidating.

"Everybody at the Clinic is so good at what they do. How do you make a suggestion to what's already the world's best? That's the mental framework. It's rather interesting and wonderful."

Central lobby

2000

FIRST BIOMECHANICALLY-ENGINEERED VALVE DEVELOPED SPECIFICALLY FOR REPLACEMENT OF THE HUMAN MITRAL VALVE WAS IMPLANTED FOR THE FIRST TIME IN THE U.S.

2003

FIRST GENE LINKED TO HEART ATTACK, CORONARY ARTERY DISEASE FOUND

Inderbir Gill, M.D.

REDEFINING

Surgery

Like ace fighter pilots, elite world-class surgeons are a breed apart. They tend to have relentlessly can-do personalities, brimming with self-confidence. And, like great sculptors or painters, they thrive on constant innovation as if responding to a genetic compulsion to continually place the bar of their personal accomplishment ever higher.

In Minimally Invasive Surgery, Less Means More

Consider the case of Inderbir Gill, M.D., a leading Clinic urologist. A native of India, he might easily have spent his entire medical career there, surrounded by a family full of doctors. Both of his parents were doctors, as well as all four of his grandparents and even several other members of his extended family. "Everybody in my family is in medicine for as far as the eye can see."

Dr. Gill was fully trained for a long career in Indian medicine, and had a comfortable life that would be the envy of most people. Still, he couldn't rest. He kept pushing himself, honing his medical skills. Which is why he first came to the United States – to pursue a fellowship in state-of-the-art American kidney transplantation procedures. But after doing perhaps 100 of these traditional open-surgery operations, he no longer felt challenged. "It had become routine," he recalls. "What turns me on is technical virtuosity!"

Then, sometime around 1990, he began to hear about some new surgical techniques that appealed to his need to be challenged: Through so-called minimally invasive surgery, a properly trained surgeon – wielding an instrument called a laparoscope, which is fitted with a tiny camera that beams video images to a screen above – could remove a patient's kidney through tiny incisions rather than the large cuts required by traditional surgery. "I thought, boy, that's got to be difficult."

He immediately wanted to learn more.

Dr. Gill, universally known as "Indy," now performs all of his surgery through laparoscopes and other minimally invasive techniques. He oversees one of the largest laparoscopic urological practices in the world, with most patients coming from outside Ohio.

"Contemporary surgery has been around for about 100 years," says Dr. Gill, who grows animated as his passion for the subject takes hold. "If, a century later, we still have to make the big cuts to effect surgical cures, we haven't really advanced a whole heck of a lot."

Where keyhole is key

Which leads us directly to the world of minimally invasive surgery (MIS), or "keyhole" surgery as it's sometimes called. This kind of surgery offers an irresistible proposition for medicine, steeped as it is in the ethos to first, do no harm. By entering the patient's body through far smaller incisions than would be required for traditional open surgery, minimally invasive procedures mean less trauma and blood loss for the patient as well as a far quicker recovery time, often just 24 hours after the procedure. And many of these surgeries can be performed on an outpatient basis.

Minimally invasive procedures range from the medically familiar to the not so familiar. Clinic cardiac surgeons have used these techniques to pioneer new ways to repair heart valves. Urologists use laparoscopic techniques to address the entire range of proce-

In a very real way,

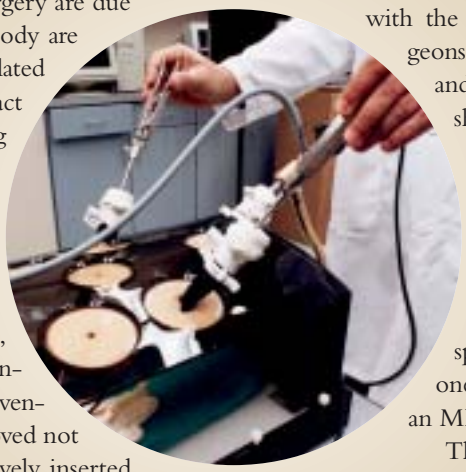
Dr. Lieberman argues, MIS techniques are as old as medicine itself.

dures in their specialty, from removing kidneys for transplantation to fixing adrenal-gland disorders. And plastic surgeons are even doing face-lifts through minimally invasive means.

"It's all about opening your medical tool box and using everything you can to reduce the collateral damage from surgery," says Isador Lieberman, M.D., the director of the Clinic's MIS Center and a staff orthopedist who has pioneered some innovative implant devices of his own to facilitate minimally invasive spine surgery (see story, page 16).

Generally, the pain and suffering from surgery are due to the trauma of entry. Organs inside the body are relatively insensitive, and can be manipulated without much patient discomfort. But the act of getting to the organ, by making those big skin cuts, putting in the retractors and moving apart muscles, that's what really hurts.

In a very real way, Dr. Lieberman argues, MIS techniques are as old as medicine itself. The first recorded minimally invasive surgery goes back more than 3,000 years, to the Egyptian Pharaoh Ramses II, who benefited from some extraordinary medical interventions for the time. His gall bladder was removed not by incision, but through a funnel imaginatively inserted into his body.



The dry lab

So, why do we care about creating newer and newer surgical techniques that, for example, can operate through a one-inch opening instead of a 10-inch opening? Consider a neurosurgical procedure once informally dubbed the "trap door," a gruesome but once necessary bit of open surgery to remove tumors behind a patient's eye. Joseph Hahn, M.D., a Clinic neurosurgeon and the founding director of the MIS Center, recounts how it would typically unfold. "We used to have to open the skull from the top, drill it out, and then our ENT [Ear, Nose and Throat] colleagues would open the side of the face to remove the tumor." Today, surgeons using minimally invasive procedures simply remove the tumor through the nostril, using a minor incision, which heals far more quickly and with far less pain than opening the skull.

But even the most avid proponents of minimally invasive surgery are careful to avoid being captured by all the excitement and buzz of the technology behind these innovations. "We have to be careful that these minimally invasive procedures stack up to the gold standard for [traditional] open surgery," says Dr. Lieberman. "We have to make sure that we're not just taking good open surgery and turning it into mediocre video-assisted surgery."

Training, collaboration and a steep learning curve

The Clinic's MIS Center, established in the mid-1990s and now located in the Emergency Services building, provides a multidisciplinary focal point for collaboration, teaching, practice and other innovations in the field. Through a joint appointment with the surgeon's primary department, Clinic surgeons from every surgical specialty can trade tips and tools in a collaborative approach. They sharpen their skills in the "dry lab," where they practice various surgical techniques for long hours, using advanced mechanical simulators developed in partnership with industry. Then they try their hand on other human substitutes at another facility elsewhere on the Clinic campus. Generally speaking, it takes a traditional surgeon from one to two years additional training to become an MIS surgeon.

The multidisciplinary character of the MIS Center was a key advantage from the outset, notes Dr. Hahn who, as chief of surgery at the time, played a central role in its founding. In an industry that's increasingly balkanized into specialties and even sub-specialties, hospitals can easily become a series of self-contained medical silos, where the urologists only talk to other urologists and cardiac surgeons and orthopaedists never trade ideas.

Says Dr. Gill, who has served a two-year stint as the center's previous director: "I think what makes our MIS Center unique is that it has all the surgical subspecialties represented – when occasions come up, we collaborate easily and readily."

At the same time, collaboration across the medical specialties doesn't preclude friendly competition between them. There is a healthy debate among Clinic surgeons, for instance, about which specialty has been more of a pioneer in minimally invasive procedures. The obstetricians/gynecologists can lay a serious claim to being among the first, since they began using early endoscopes to perform pelvic exams and surgeries as long as 15 years ago (one

of these early devices, in fact, now resides in the Smithsonian Institution in Washington, D.C.). And their colleagues in orthopaedics have been using video-enhanced instruments to conduct arthroscopic knee surgery, a cornerstone procedure, since the 1970s.

MIS has a reputation in the medical community for being difficult to learn, "And rightly so," concedes Dr. Gill. "But it's all a mindset. We feel that you can learn it, but like anything else, you've got to put in the work, the effort." If a traditional surgeon came and spent a year with his group, watching and learning, "they'd be ready to rock and roll" on their own, he says.

Actually, there is a steep learning curve for those who trained in the traditional surgical fashion, where the medical phrase "laying on of hands" wasn't mere metaphor. "Thirty years ago, when I was in training," says Dr. Hahn, "you had to make a hole big enough to see it, to feel it, because the idea then was to do everything by feel, to get in there and get around it. And with some of the abdominal surgeries, that was a heck of a big hole." With these new procedures, he says, "if you're not facile, and have great depth perception, it is incredibly hard. Some people will never get the hang of it."

One of the simplest but most disorienting differences is that traditional surgeons look down at the body, while in MIS the surgeon is looking up at a screen. "I'm operating down here, but I'm looking up there – that's the disconnect," Dr. Gill explains. "But once you've done enough of these, it just becomes second nature."

Dr. Gill performing surgery

Dr. Lieberman, who was first recruited to the Clinic as an MIS specialist, thinks these techniques will take root naturally. For surgeons now in training, minimally invasive techniques are simply being integrated into the curriculum, and every young surgeon will learn them as a matter of course. As a largely self-regulating industry, the governing societies of some surgical specialties are beginning to craft formal guidelines, mandating that a student must see a certain number of patients or perform a certain number of cases before they can call themselves minimally invasive surgeons. But Dr. Leiberman thinks the fear of these techniques will quickly dissolve as the procedures continue to work their way into the fabric of medicine.

"Surgeons are surgeons because they have this ability to synthesize a picture in three dimensions," he says. "Some people are all thumbs. But others, like those who become surgeons, have great manual dexterity. There's almost a genetic selection to becoming a surgeon. And those are probably the same people who are good at video games."

Beyond MIS

The pace of surgical innovation is quickening: The video cameras and other instruments keep getting smaller and the resolution better. "One of the limitations of this surgery is still that we're working in a two-dimensional area," says Dr. Lieberman. But with ever-enhanced magnification, "as you get closer to the microscopic level, the possibilities keep expanding."

But the smaller cut – or increasingly mere needle punctures – is by no means the endgame in innovative surgery. In fact, some at the Clinic would call it medicine's present, with non-invasive procedures constituting the future. The use of biologics and radio frequencies are among the most promising of these emerging areas.

Biologics involve harvesting a patient's own stem cells to re-grow native body tissues. The technology is already widely used in some areas of surgery, and is expected to spread to many others. "We're already doing that with spinal-fusion surgery," says Dr. Lieberman. "It's completely eliminated bone-grafting procedures." Other possible applications are nearly endless. In the case of treating burn patients, "maybe we can give the patient back their own skin, instead of doing a skin graft from another part of the body," notes Dr. Lieberman. And orthopaedists are eager to use the technology to re-grow a patient's damaged knee cartilage.

Beaming frequencies from outside the body to effect internal therapy is another promising area. The technology is already being used in breaking up kidney stones and soft tumors without the need for any incision, "but it doesn't take a lot of imagination to see how that can be used in other ways," says Dr. Lieberman.

Robotic surgery technology raises the specter of a doctor in, say, Cleveland, remotely operating on a patient halfway around the globe. While there are some remaining hurdles (including those of cost), it's yet one more possibility for the future.

In the end, perhaps the most heartening development in all these technical advances in surgery has little to do with technology. Taken together, they move everyone closer to an elusive goal in medicine: radical simplicity. By increasingly allowing pioneering practitioners to think outside traditional boxes as they seek to forever drive down the costs, pain and recovery time of surgery, these innovations are helping to deliver a pleasing new paradigm for medicine.

"I have a talk I give on what the surgery suite of the future will look like," says Dr. Hahn, who adds that he brings along a visual prop to drive home his point. "It's a picture of my office." ■

Peter K. Kaiser, M.D., *Retina Specialist at the Cole Eye Institute,*
answers questions about

Age-related Macular Degeneration

Age-related Macular Degeneration (AMD) affects more than two million Americans each year and is expected to explode as the population ages. The exact cause of this eye disease is unknown and currently there is no cure. However, new studies using new and existing drugs and treatments mean AMD sufferers have hope of seeing a better future.

Q: What Is Age-related Macular Degeneration? What causes it?
A: AMD is a disease that can blur the sharp, central vision you need for important activities such as driving and reading. As patients age, the macula, which is the central part of the retina, begins to deteriorate and becomes less able to get rid of waste products. This may cause a thickening in some of the layers in the macula, which leads to vision problems. AMD has two different forms: wet and dry. Both can lead to loss of the central vision, although neither one usually causes complete blindness. Wet AMD is more severe than dry AMD.

Q: What's the difference between wet and dry AMD?
A: Patients with dry form AMD start to develop yellow deposits – called drusen – under the retina and atrophy in the macula. The most common symptom is slightly blurred vision. Most patients with drusen never develop AMD. However, some patients with drusen will develop AMD. Dry AMD is characterized by thinning of the macular cells. Wet AMD occurs when abnormal blood vessels grow from outside the retina inwards and underneath the macula. They bleed, leak fluid and eventually cause scarring, which leads to permanent loss of central vision.

Q: What causes AMD to degenerate from dry to wet?
A: In general most patients don't progress from dry to wet AMD, but 15 to 20 percent of patients will progress to wet AMD. We don't know exactly what causes the progression. We're looking at what triggers the eye to start breaking down and developing abnormal blood vessels. We don't know why drusen form or how that leads to increased risk for wet AMD. These are things we're working to determine.

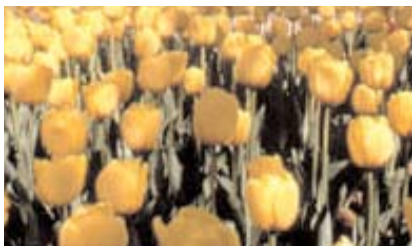
Q: Who gets AMD? What are the signs?
A. Two hundred thousand new cases of wet AMD and two million cases of dry AMD are diagnosed each year in the United States. AMD affects both men and women and is the leading cause of vision loss in people 50 years of age and older. AMD doesn't cause any pain and, in some cases, it advances so slowly that people don't notice a change in their vision. In other people, the disease progresses faster and may lead to a loss of vision in one or both eyes.

Q. What are the tests used to diagnose AMD? How can you tell if it's getting worse?
A. The most common test to diagnose wet AMD is the fluorescein angiogram. A colored dye is injected into a peripheral vein and then a special camera is used to photograph the back structures of the eye.

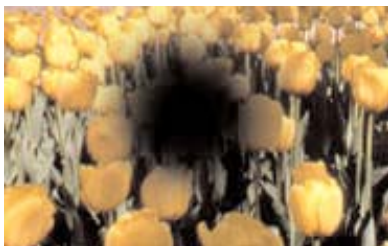
People with macular degeneration can check their own vision with a simple test called the Amsler grid. The patient looks at a large dot in the middle of the grid and notices any areas where the lines look blurry, wavy or broken. If the grid lines seem to be more distorted than before, it might be a sign that the macular degeneration is getting worse and needs treatment. The patient should immediately get an eye examination when this occurs.

Q: While there is no cure for dry AMD, what treatments are out there to slow or stop its progression?
A: Once dry AMD reaches the advanced stage, no form of treatment can prevent vision loss. But vitamin treatment can delay and possibly prevent some patients with drusen from going to the advanced stage where vision loss occurs. The National Eye Institute's Age-Related Eye Disease Study (AREDS) found that taking a specific high-dose formulation of antioxidants and zinc reduces the risk of advanced AMD and associated vision loss.

Q: What are some treatments for wet AMD?
A: We often use photodynamic therapy. A drug called Verteporfin is injected into your arm. It travels throughout the body, including the new blood vessels in your eye. The drug tends to "stick" to the surface of new blood vessels. Next, a light is shined into your eye for about 90 seconds, activating the drug. The activated drug destroys the new blood vessels



NORMAL VIEW



TWO VIEWS WITH AMD

and leads to a slower rate of vision decline. Unlike laser surgery, this treatment does not destroy surrounding healthy tissue. It's important to remember that photodynamic therapy slows the rate of vision loss, but it doesn't stop vision loss or restore vision in eyes already damaged by advanced AMD. Treatment results often are temporary; you may need to be treated again.

We're studying a few things to modify photodynamic therapy to improve its outcomes and we're doing several smaller trials to improve its effectiveness. We also have some other trials under way to test uses that weren't specifically tested and approved by the FDA-approved trials, called "off-label" uses. And we're looking at the use of anti-angiogenic drugs, drugs that block the growth of the abnormal blood vessels, in several clinical trials. Finally, in some patients, laser treatment or surgery can be beneficial.

Q: What hope is there for a cure?

A: All areas of AMD are undergoing intense research here at the Cole Eye Institute with particular emphasis on wet AMD, where the most vision loss occurs. We're studying how to prevent vision loss and prevent new blood vessels from forming. We're studying what causes vessels to grow so we can stop them from growing. And we have a number of studies and clinical trials taking place.

One class of drugs that we're looking at is the anti-VEGF inhibitor drugs. VEGF is a growth factor that causes blood vessels to grow and studies have shown that anti-VEGF can be used to block and prevent these blood vessels from growing. We're testing two different drugs that block blood vessels from growing in the eye – Macugen and Lucentis. Macugen blocks one specific form of VEGF and Lucentis blocks all forms of VEGF from causing blood vessel growth. In both the Macugen and Lucentis studies, it appears that the drugs are preventing growth and vision loss in people with wet AMD. These two studies are ongoing.

Additionally, we're conducting a study using Retaane. This drug blocks the growth of blood vessels in a different way. It's a new class of drugs called cortisene drugs. Retaane is administered around the eye every six months and works downstream of the growth factors like VEGF. If you look at how blood vessels grow – growth factors stimulate the cell to grow – Macugen and Lucentis block the growth factor. They stop VEGF stimulation, so there's less growth of blood vessels. But there are multiple growth factors. Retaane works inside the cell no matter what the growth factor. Testing is ongoing right now to see if this drug works better than the other drugs.

We're also studying the use of Retaane as an inhibitor for dry AMD. It's called the Antecortave Acetate Risk Reduction Trial (AARRT). We're taking patients with dry AMD and giving them an injection once every six months for four years while monitoring their vision to measure any changes, and to see if we can prevent these patients from ever developing wet AMD.

Q: Until we have the results of all these studies and have developed treatments from them, what can people do to protect their vision?

A: Lead a healthy lifestyle. Don't smoke. Eat healthy. Specifically eat a lot of green, leafy vegetables and pigmented fruits like oranges, kiwi, spinach and carrots. Wear UV eye protection. Reduce your cholesterol. I strongly recommend that everyone over age 50 get checked yearly for AMD by an ophthalmologist.

To learn more about AMD, go to:
www.clevelandclinic.org/clevelandclinicmagazine

FORMER AMBASSADOR TO AUSTRIA HONORS INSPIRATIONAL LIFE OF WIFE

Ambassador Milton A. Wolf, Ph.D.

commits a $2 million gift to support the Heart Center in memory of his wife Roslyn.

To honor his wife and her life's work, Ambassador Milton A. Wolf has made a $2 million commitment to the new Cleveland Clinic Heart Center. His contribution will continue the humanitarian work Roslyn Z. Wolf cherished throughout her life.

Together, the Wolfs used their talents and energies to effect change across international boundaries. While he is best known for his part in organizing the Strategic Arms Limitation Talks (SALT) II, during his lifetime Ambassador Wolf has held many local, national and international leadership roles. Currently he is a governor of the United Nations Association of the U.S.A.; a chairman of the American Austrian Foundation; a former chairman of the Board of The Ohio State University;a member of the Board of Directors of the Institute for the Study of Diplomacy at Georgetown University; and Co-Chairman of the Council of American Ambassadors. In addition to these responsibilities, the ambassador is chairman of Milton A. Wolf Investors, a private investment firm, and serves as a Cleveland Clinic trustee. A published economics expert, Ambassador Wolf has earned four degrees, including a Ph.D. in economics from Case. He also has been awarded several honorary doctorates and has been hooded a fellow of Brandeis University.

Yet, for all his accomplishments, Ambassador Wolf's favorite memories stem from his marriage to Mrs. Wolf, who passed away in 2001. "One of the most wonderful moments in my life was meeting and marrying Roslyn Zehman," he says. "She was the finest person I ever met; she brought sound judgment and equilibrium to my life."

Ambassador Milton A. Wolf, Ph.D. and his wife Roslyn in 1979.

As wife of a United States ambassador, Mrs. Wolf was frequently called upon to entertain statesmen from all over the world and she held many important positions in local and national organizations. Yet in a recent biography, she updated her file only to say that she was a "volunteer."

"This remarkable modesty was one of Roz's exceptional qualities," says Ambassador Wolf. "She was a great humanitarian, chairing many groups, volunteering her help to many organizations. Yet for all she did, she never sought recognition."

Mrs. Wolf, an active community volunteer, was greatly admired for her straightforward yet modest manner and ever-flowing compassion. In a tribute to Mrs. Wolf, fellow Jewish Community Federation of Cleveland members noted, "She had the qualities that inspired us, that quietly held us to a higher standard. That made Roz one of the most dearly loved persons in our midst." Mrs. Wolf was elected a life trustee of the organization shortly before her passing.

Ambassador Wolf in 1979 at the SALT II talks with U.S. President Jimmy Carter and Soviet President Leonid Brezhnev.

In 1977, Ambassador Wolf accepted the position as ambassador to Austria after declining other senior positions offered to him by former President Jimmy Carter. At the time, Austria was a neutral country on the edge of the Iron Curtain and it became a bridge between the East and the West. During his tenure, Ambassador Wolf organized the 1979 SALT II talks in Vienna, bringing President Jimmy Carter and Soviet President Leonid Brezhnev together for the first time. Additionally, Ambassador Wolf handled matters ranging from bilateral negotiations between Austria and the United States, to multilateral trade treaty and maritime shipping negotiations.

However, in his weighty role Ambassador Wolf did not serve alone. In her home, Mrs. Wolf entertained many esteemed guests, including President Carter, Henry Kissinger, Yitzhak Rabin and Brezhnev. Gracious and straightforward, she hosted those political titans with all the diplomacy and dignity of an ambassador herself. In an additional capacity, she also chaired the Committee of 110 Ambassador's Spouses in Vienna.

Austria has embraced the couple's charm and diplomacy, endeavoring to pay them homage. Ambassador Wolf became the only sitting ambassador to receive the Great Gold Medal of Honor with Sash, Austria's highest decoration. Mrs. Wolf will soon be honored in Salzburg. The gardens and park surrounding the magnificent 14th century Schloss Arenberg - summer residence of the Vienna Philharmonic Orchestra and an international meeting place for artists, musicians and scientists – will be named in her memory.

Minimally invasive means *"miracle"* to Lucius B. McKelvey.

Lucius B. McKelvey

For most days of the month Lucius B. McKelvey feels great. The other days he's a little tired. That and a tiny scar are the sole reminders that he once had a large tumor in his brain. Thanks to the Brain Tumor Institute, the 58-year-old Mr. McKelvey has reached his 18th month of recovery.

Despite the few days of fatigue his oral chemotherapy treatment causes, Mr. McKelvey enjoys life now more than ever. In addition to business meetings, his days include hugging the back roads on his Harley-Davidson motorcycle and handcrafting wood in his barn. He takes vacations from his post as chairman of Smythe, Cramer Co., a leading Cleveland real estate company, to visit Nantucket, Massachusetts and Naples, Florida with his mother. He also spends more time with his grandchildren.

His life changed dramatically after suffering a massive seizure. He was rushed to a local hospital where doctors could not identify the seizure's cause. A family friend proactively sought Mr. McKelvey's transfer to The Cleveland Clinic, where, within 24 hours, he underwent expert diagnosis and surgery to remove a brain tumor. Through a 1.5-inch opening, Gene Barnett, M.D., chairman of the Brain Tumor Institute, used computer navigation equipment to guide him in removing most of the tumor.

"What The Cleveland Clinic calls minimally invasive, I call a miracle," says Mr. McKelvey. He is grateful for Dr. Barnett's skilled hands, and for the physician's sensitivity and communication skills. Mr. McKelvey also recognizes the quality follow-up care provided by the entire medical team, from assistance with his recovery to close monitoring of his chemotherapy treatment. At every turn, they have shown kindness and sensitivity, and made themselves available to address questions and concerns in layperson's terms, he says.

To show appreciation for the compassionate, life-saving care he has received, Mr. McKelvey offers his philanthropic support for research, learning and innovation at the Cleveland Clinic Taussig Cancer Center and the hope to further refine the miracle of Cleveland Clinic brain surgery. His $1 million gift to create the Sallie Turner McKelvey Endowment Fund, named for his mother, was made in honor of Dr. Barnett's expert care. Mr. McKelvey's gift and leadership as chairman of the Brain Tumor Institute National Leadership Board will help the Brain Tumor Institute pioneer surgical procedures, develop imaging techniques, investigate possible treatments and, ultimately, save lives.

FIRST ENDOWED TECHNOLOGY TRANSFER PROGRAM IN U.S.

John and Sharon Ferchill

make a lasting gift to grow innovation and employment.

John and Sharon Ferchill

In 1982, John and Sharon Ferchill created the Jennifer Ferchill Foundation in honor of their daughter who died of a rare brain tumor at the age of nine. Through the years, the foundation has contributed to programs that benefit children, provide assistance to families with sick children and support education through scholarships. The Ferchills also have contributed to the construction of a rooftop playground at the Cleveland Clinic Children's Hospital.

Most recently, the Ferchills have offered a generous $5 million donation that will be used to create a new center for biomedical innovation and technology transfer. This center will focus on turning medical discoveries into commercial products that directly benefit patients. The new Ferchill Center for Innovation and Technology Transfer at The Cleveland Clinic is believed to be the first technology transfer program in United States history that has been philanthropically endowed. The new center will be part of CCF Innovations (CCFI), the Clinic's technology commercialization arm (see article, page 16).

The Ferchills first met Joseph F. Hahn, M.D., during their daughter Jennifer's treatment at The Cleveland Clinic. They later became interested in CCFI when Dr. Hahn was named its chair. Their donation will be used to endow the CCFI chairmanship. In addition, their donation will establish an annual "Ferchill Award" given to the inventor whose product has had the most impact on the Cleveland community.

Mr. Ferchill says that the goal of the donation is not about funding one particular area of research – such as finding a cure for cancer – but about promoting the future of bioscience and medical innovation in Cleveland and making a powerful impact on the area's economy. Their donation will help CCFI grow so that it brings more jobs to the Cleveland area.

"As we have grown the foundation and looked at what we're trying to accomplish, we have figured out that one of the most important things children need is a stable family with parents who have jobs," Mr. Ferchill says. "We truly believe that the Clinic is the single best place to create jobs and that CCFI is the focus of that job creation."

INVACARE LEADERS SEE A BRIGHT FUTURE

Health care visionaries give

$7.5 million for new Heart Center.

Joseph B. Richey II and A. Malachi Mixon, III

In 1979, a salesman and an engineer pooled together $1.5 million of equity to purchase a small wheelchair manufacturer called Invacare for $7.8 million. Over the next two and a half decades, A. Malachi Mixon, III, chairman and CEO of Invacare Corporation, and Joseph B. Richey II, president of Invacare Technologies Division, transformed the sleepy little company into a global force within the home health care market. In 2003, the FORTUNE 1000 company in Elyria, Ohio, posted sales of $1.25 billion.

Recently, in an action that parallels their initial jump-start of Invacare, Mr. Mixon and Mr. Richey, together with their company, committed a total of $7.5 million to The Cleveland Clinic. Their gift will help build the new Cleveland Clinic Heart Center, which the business partners believe is critical to the future of the Clinic and their home base of Northeast Ohio.

Mr. Mixon, who also is chairman of the Board of Trustees of The Cleveland Clinic, says, "I think I can speak on behalf of the Clinic trustees that we must provide the best, state-of-the-art facilities, equipment and capability for these great physicians to continue to be number one."

Offering more than a keen sense for successful health care strategies, Mr. Mixon and Mr. Richey have influenced the way physicians practice medicine. As an engineer at Ohio Nuclear, Inc., in Solon, Ohio, Mr. Richey developed the first commercial full-body CT (computed tomography) scanner, which gave physicians their first noninvasive view into the body. The prototype was installed at the Clinic in the 1970s.

Mr. Mixon led Ohio Nuclear's marketing of the CT machine that made liver tumors "light up" before physicians' eyes, and Mr. Richey went on to develop a full-body MRI (magnetic resonance imaging) scanner. It was an exciting time in medical imaging and many were surprised when Mr. Mixon and Mr. Richey gave it up for the seemingly low-tech wheelchair market.

But in the early 1980s, when power wheelchairs depended on cumbersome, unreliable technology, Mr. Richey, who is always looking ahead to the next challenge, saw an engineering opportunity. At Invacare, he incorporated microprocessor controllers in wheelchairs, forever changing the market. His most recent innovation is a portable oxygen system called HomeFill II that manufactures oxygen from the air in a person's home and fills cylinders for ambulatory oxygen use.

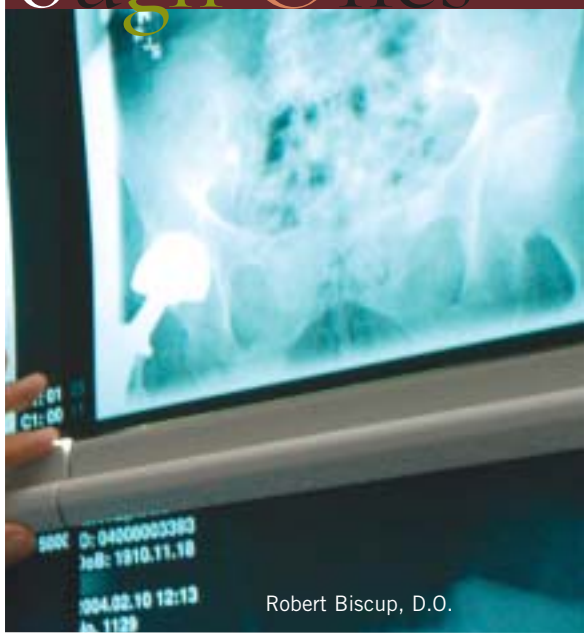
"When you go into a field and you see what they have and know you can make it a lot better, it's just fun to do it," says Mr. Richey, who recently joined the Clinic Board of Trustees.

Mr. Richey and Mr. Mixon also are generous in lending their expertise to others in the medical innovations field. After meeting an inventor with an idea for a new approach to sterilization, for instance, they helped start Steris Corporation, now another global health market leader based in Northeast Ohio. Mr. Richey still serves on the Steris Board of Trustees.

While their talents could be applied in practically any industry, innovating in health care is a natural fit for these business partners. "I think we both have it in our blood, and health care is such a satisfying field – to do the things that we've done," says Mr. Mixon.

"And by the way, we plan to continue to develop exciting new medical products as long as The Cleveland Clinic continues to keep us kicking," adds Mr. Richey.

Only the Tough Ones



Robert Biscup, D.O.

For 13 years

Joan Smith★ of Alabama endured agonizing back pain. Several costly, unsuccessful surgeries only compounded the problem. Not only did Smith's bank account dwindle with each procedure, but she grew extremely depressed and addicted to a painkiller. Worst of all, her posture deteriorated so badly, she could barely function: By the time she arrived at Cleveland Clinic Florida's Spine Institute to see Robert Biscup, D.O., her body was bent forward and twisted to the right. Disheartened, Smith viewed the Spine Institute as her last hope.

Tom Stevens★, a 16-year-old from West Virginia, suffered from spondylolisthesis, an acquired deformity in which a stress fracture in the vertebrae causes the spine to shift out of place. Consequently, Stevens' buttocks jutted up and out, creating a giant bubble effect. In addition to looking odd, the teenager was depressed, weak and could barely walk because of nerve problems in his legs. He'd undergone two unsuccessful surgeries by the time his family ended up at the Spine Institute. Like Smith, he too was desperate.

"Our patients come to us emotionally, mentally and physically debilitated," says Dr. Biscup, chairman and director of the Spine Institute, which is located in Naples, Florida. "These are the patients that can't get out of bed, can't exercise and often have serious neurological problems. Some of them are deformed to the point where they can't stand up without falling over. Oftentimes we are the last stop – the final resort," he says.

Biscup, a no-nonsense, silver-bearded physician whose intense expression conveys how seriously he takes his work, specializes in spinal surgery – including major reconstructive spinal surgery, spine surgery that had failed, and minimally invasive spine surgery. Appointed to The Cleveland Clinic in 1997, Dr. Biscup is on staff in the neurological surgery and orthopaedic surgery departments in addition to the Spine Institute. Previously, he practiced orthopaedic spinal surgery in the Cleveland area where he participated in cutting-edge research. Currently he's internationally recognized as a pioneer in the field of spine care and spinal surgery.

Dr. Biscup launched the Cleveland Clinic Florida Spine Institute – which includes a center for spine surgery that has failed – a year ago to handle the tough cases other spine centers cannot. It's just one of a handful nationwide equipped to deal with the complex problems of patients who continue to experience pain and disability after back surgery. It's also the only center in South Florida able to perform minimally invasive spine surgery, which results in expedited recovery times. Both Dr. Biscup and the Spine Institute's Robert Isaacs, M.D., are active in outpatient microsurgery, which involves tiny, rather than large, incisions.

"Patients are often told they need a major operation with fusions and rods followed by five days in the hospital, when all they really need is a one-inch incision that takes a half-hour and lets you walk the same day," Dr. Biscup explains.

Besides failed back surgery, the comprehensive institute deals in all matters relating to spinal medicine and surgery. But what truly sets it apart from other centers is its team approach toward treatment, in which patients' needs are met by a team of specialists representing various medical and therapeutic disciplines. As a part of the team – which includes spine surgeons, medical spine doctors, intervention pain specialists, physical therapists, psychiatrists and psychologists – each specialist assesses the patient, and then, as a group, the members determine a patient's best course of treatment. Some patients may need surgical treatment, others physical therapy and help with drug addiction. Still others may need an altogether different treatment protocol.

"We developed this team concept because I don't believe a surgeon alone is capable of evaluating a complex case such as a spine surgery that has failed," says Dr. Biscup. "Not only do you have to look at a patient's anatomy, but you also have to consider their ability to function, physical therapy needs, pain management, how they feel about themselves, if they're sleeping well, and how to keep them healthy overall."

Now under construction at the Clinic's Weston campus is a space designed to complement this team approach, with areas for physical therapy (which includes using golf and other recreational sports as part of physical therapy), testing, research and more. Patient exams will take place around a central area nicknamed "The Bone," because it is indeed bone-shaped. Here, four doctors will be able to work together at the same time with patients in a relatively small area, while simultaneously interacting with each other.

"The benefit here is that we can work as a team with curbside consulting," Dr. Biscup explains. "In other words, we won't have to send patients home with referrals and make them drive back and forth. Some patients live two hours or more away. And a lot of our patients are from out of state."

> "Patients are often told they need a **major operation** with fusions and rods followed by five days in the hospital, when **all they really need** is a one-inch incision that takes a half-hour and lets you walk the same day."
> —Robert Biscup, D.O.

Surgical Technician Danielle Ernst and Physician's Assistant John Booher assist Dr. Biscup (middle) with microdecompression surgery.

The center for spine surgery that has failed already has helped more than 100 patients, including William Smart*, a high-profile Midwest executive who had undergone a harrowing seven unsuccessful back surgeries before turning to the institute. He was in terrible pain, addicted to narcotics, depressed and had very low self-esteem. It also had affected relations with his wife and family and his ability to function in his high-profile position.

"When he came to us, he said that all the other doctors he'd seen told him nothing more could be done to help," Dr. Biscup says. "I did an assessment and saw that there was still a problem anatomically, and that this very likely was causing his pain. He met with members of our team and it was determined he needed surgery. We did the surgery. Then it took us, as a team, over a year to get him through, and ultimately off the medication. But he healed properly and today lives relatively pain free."

Dr. Biscup recalls seeing Smart smile for the first time. "Prior to the surgery his smile was always forced. He was always wincing," he says. "Then about three months after his surgery I saw him smile. He told me that it was the first time in nine years that he didn't have back pain. That was a good day."

Though a serious man of science, Dr. Biscup admits to shedding the occasional empathetic tear. Two days after performing surgery on Joan Smith, she was able to stand tall for the first time in 13 years. "It was very emotional for her," Dr. Biscup recalls. "She was crying and saying how happy she was that someone was finally able to help her. And I wiped a few tears with her."

Dr. Biscup also was able to help teenager Tom Stevens. "This is a kid who was very quiet," Dr. Biscup says with a laugh. "But the last time I saw him he said that if I was a woman he'd give me a big, sloppy kiss."

**Names changed to protect patient confidentiality.*

THE TRANSPLANT CENTER'S DEDICATED Duo

When Jennie Foertch, R.N., and Alan Stewart, R.N., walk through the waiting room of the Transplant Center, the eyes of former patients light up. Hands wave and smiles brighten faces as the two stop for a quick chat, offering a pat on the knee and a word of encouragement.

Cleveland Clinic Lung Heart/Lung Transplant Coordinators Foertch and Stewart are a dedicated duo, a pair who help save lives for a living. From the time a patient is first referred until the day of transplant, these two stay involved, getting to know each patient, seeing them bi-monthly for checkups, becoming friends. The work is non-stop. They put in long hours with very little sleep.

And they love it. "On Friday nights, we say: 'Only two more working days until Monday,'" jokes Stewart.

But the long hours are no joke. These two are "on call" for donors and transplant recipients around the clock. When a donated organ becomes available, they begin a series of phone calls that are just the start of the exacting process of coordinating all the teams necessary for the success of a transplant.

Lining up the transplant team, chartering jets and ambulances, and making sure the operating room and staff are ready are just a few of their long night's tasks. "If we are working two or three transplants at once, we are setting up six or seven planes at a time," says Foertch. There is a four-hour window between the time the donated organ is removed and when it must be transplanted. "The clock starts ticking when they clamp the aorta," she says. "It's a fine art to try to time it perfectly." She adds with a smile, "It's organized chaos."

Transplant Center Administrator Art Thomson says Foertch and Stewart are typical of all the hard working folks in The Cleveland Clinic's transplant programs. "They are a highly qualified, passionate, extremely dedicated lifeline for the patients. You wouldn't find many people who get enthused about being up all night coordinating transplants," says Thomson.

If a call comes in the middle of the night, they immediately rush into their home offices where a bank of phones, a computer and fax machine crank up. "We can be on the phones for eight hours at a time, dealing with the donor center, getting lab updates," says Stewart.

"Sometimes we can't even drive into work because there is so much phone action," says Foertch. "I've had to pull my car over and do business from the parking lot of a McDonald's or Giant Eagle."

Informing a wait-listed patient that his or her time has come is a thrill for Foertch. "It's exhilarating to make the call. It's my favorite part."

There are hours of boredom and moments of panic, says Foertch. "Afterwards you are either dead tired and ready to sleep or your adrenaline is so high you can't sleep."

The two have files of thank-you notes and they find the accolades amazing. "Our patients say 'thank you' so much and we're just doing our jobs," says Foertch. "It's touching. We're just the worker bees, the middlemen."

Fifty-nine year old Fred Saleman was on the receiving end of one of Foertch's calls. Saleman and his wife, Mary Joyce, flew in from New York and a few hours later he was in the operating room sedated. Within seconds of removing his lung, a call came informing the doctors that the donor had cancer and the lung could not be used. The medical team kept Saleman stable and under sedation, all the while doing something they had never done before. "We put out an 'urgent need' call," says Foertch. "These sorts of calls are often used in heart and liver transplants, but not in lung transplants."

After contacting all the Ohio organ procurement organizations, the team found a donor. Forty-eight hours later, Saleman had a successful operation. He knew nothing of the efforts under way on his behalf. "I just took a nap for a couple of days," he jokes. "But my wife saw it all."

For Foertch and Stewart, it was just another roller-coaster day at the office.

Alan Stewart, R.N. and Jennie Foertch, R.N.

Feed a Blood Vessel, Starve a Tumor


Qing Wang, Ph.D.

As far as Qing Wang, Ph.D., is concerned, sometimes you *can* have it both ways.

Groundbreaking genetic research by Dr. Wang, director of the Center for Cardiovascular Genetics and staff member in the Department of Molecular Cardiology, and his team may lead to the development of medication therapies that would spur the growth of new blood vessels to treat heart and stroke patients. Alternate therapies derived from the same research could also be used to block the growth of new blood vessels that feed cancerous tumors, leaving them to starve to death.

The growth of new blood vessels, called angiogenesis, is an important natural process, both in health and disease. But in many serious disease states, the body loses control over angiogenesis. Insufficient angiogenesis occurs in diseases such as coronary artery disease, stroke and delayed wound healing. In these conditions, inadequate blood vessels result in poor circulation and the risk of tissue death.

Excessive angiogenesis occurs in cancer, age-related macular degeneration, rheumatoid arthritis and more than 70 other conditions. In these conditions, new blood vessels feed diseased tissue, destroy normal tissue and, with cancer, nourish tumor cells with oxygen and nutrients.

In 1999, Dr. Wang discovered the gene VG5Q, which is believed to trigger Klippel-Trenaunay Syndrome (KTS), a rare congenital vascular disease. After identifying VG5Q, Dr. Wang and his research colleagues spent the next four years studying, observing and learning how the gene functions.

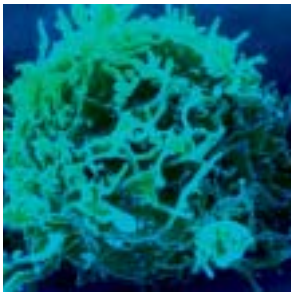
Dr. Wang's team found that purified VG5Q protein can promote new blood vessel formation, and a certain mutation of the VG5Q gene in KTS patients can further increase blood vessel formation. This important discovery could help future generations of heart disease patients. If a cardiologist determines that a person's heart blood vessels are partially blocked, a medication made from the VG5Q gene or protein could grow new blood vessels and prevent a potential heart attack. The ability to grow new blood vessels also might prevent patients from suffering strokes or delayed wound healing.

In additional research, by using a small molecule called siRNA, Dr. Wang and his researchers were able to knock down the level of VG5Q protein in cells, and that successfully blocked the formation of new blood vessels.

"We're very excited about this because for a tumor to grow, or for a tumor to move to other parts of the body, it needs new blood vessels that provide the tumor with oxygen," Dr. Wang says. "The idea is if we can block the blood vessel formation in tumors by destroying VG5Q in blood vessel cells, the tumors will die."

Dr. Wang's research on the VG5Q gene was published in the February 12, 2004 edition of *Nature*. He believes that the final goal of developing medications to grow or block blood vessels may be achieved within five to ten years.

Fighting Tumors That Fight Back


T lymphocyte

Researchers at The Cleveland Clinic were among the first to discover that tumors kill T lymphocytes. T lymphocytes, or T-cells, are part of the body's natural immune system and help protect against diseases such as cancer. Today, Clinic researchers, led by James H. Finke, Ph.D., a research immunologist, are trying to find out how to help those T-cells fight back so that they can effectively kill cancer cells.

T-cells are an important component of the body's immune system to protect against infectious diseases and cancer. They do this by recognizing antigens that are foreign to the body and destroy the cells containing these antigens.

"But what we found is that when the T-cells enter the tumor in response to the antigen recognition, the T-cells are being destroyed rather than the tumor being destroyed," says Dr. Finke. "The tumor fights back by somehow triggering T-cell death through a process called apoptosis, programmed cell death."

Dr. Finke says his research is focused on uncovering how tumors induce T-cells to die. "We want to find out how we can stop or block this T-cell death from happening so that the T-cells can do their job of getting rid of the cancer," he explains.

He believes that additional research efforts will eventually lead to a new treatment that will include a combination of a vaccine to stimulate T-cell activation and drugs that can protect the T-cells from the harmful effects of the tumor. "We've made significant progress in understanding how tumors impact the immune system, but there's more work to be done," Dr. Finke adds.

He hopes that clinical trials may get under way in the next three to five years. Although the current research is focused on kidney cancer, Dr. Finke also hopes that the new approach would be useful in fighting other types of cancers.

Waking Sleeping Kidneys

Acute renal failure (ARF), the sudden loss of kidney function, affects up to seven percent of patients in a hospital and 30 percent of intensive care unit patients. Blood loss from a surgery or major injury, dehydration or even some medications may shut down the kidneys. Treatments such as dialysis can help replace kidney function, but in some patients a long delay may occur before kidney function returns.

Emil Paganini, M.D., section head of Dialysis and Extracorporeal Therapy, in collaboration with H. David Humes, M.D., of the University of Michigan and other researchers, has helped to develop a new renal assist device (RAD) that may lead to new treatments for ARF patients as well as to treatments for those patients who also suffer from infection and chronic renal failure.

Last year, 10 ARF patients from Ohio and Michigan were treated with the bioartificial RAD, which exposes the patient's blood to new human kidney cells across an artificial membrane. This exposure allows the RAD cells to produce substances that can "talk" to the dormant kidney and other organs, perhaps replacing important but missing signals. This treatment saved 40 percent of the patients and was considered a success by researchers and federal regulators. Now, Dr. Paganini is leading Phase II of new FDA-approved trials that will include at least 12 ARF patients at The Cleveland Clinic and perhaps two dozen more patients at four other sites in the United States.

"We're using living cells as metabolic units to mimic what the natural kidney does," says Dr. Paganini. "We know that these cells produce a lot of things like vitamin D, and they help break down insulin. However, the endocrine function of the kidney is only partially understood. One thing we do know is that adding new cells via the RAD system will help the endocrine function of the kidney." While the kidney's main job is to remove waste from the body, its endocrine function also produces certain hormones that can affect other organs in the body.

Inside the renal assist device, artificial fibers contain human kidney cells.

"We are applying the RAD technique to ARF patients to see if we can make the kidney come back faster," Dr. Paganini says. "This will tell us whether there are signals that the sleeping kidney needs to wake up. Some of those signals may be applicable in patients who have failing kidneys or chronic renal failure."

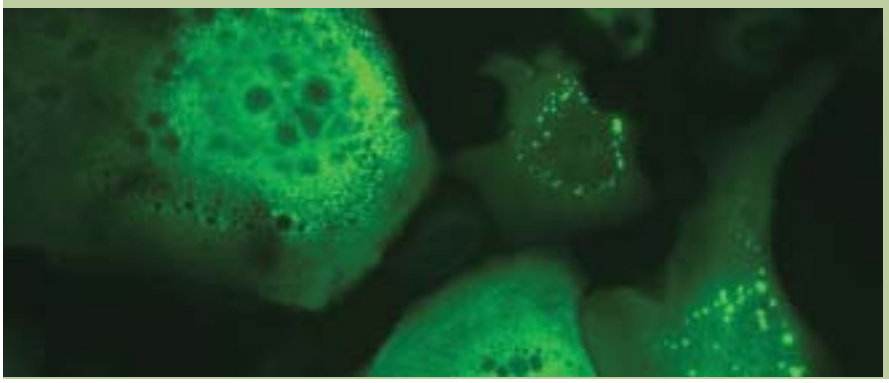
Future Hope for Cystic Fibrosis Patients

About 50 percent of babies born with cystic fibrosis (CF) are hospitalized in the first year of their lives, and their average life expectancy is only 30 or 40 years. CF is a chronic, progressive and fatal genetic disease associated with abnormalities of mucus in the lungs. For patients with CF, the chemical properties of mucus become altered and the lungs become susceptible to infection. Over time, recurrent infections destroy the lungs.

"It's a debilitating and life-threatening problem," says Serpil Erzurum, M.D., whose specialty is pulmonary critical care and research in this field. "Our hope is that through our research we will find new clinical therapies that can give these individuals a normal lifespan."

Last year, Dr. Erzurum's dream took its first major step toward that goal. Her research, performed in collaboration with researchers Bryan Williams, Ph.D., and Jaharul Haque, Ph.D., and with former Cleveland Clinic researcher Shuo Zheng, Ph.D., determined that a defective molecular mechanism made CF airway cells more vulnerable to viral infection during the first two years of life. Dr. Erzurum's research was published in the journal *Immunity*.

When the cells in the human body are exposed to a viral infection the cells make a defensive gas called nitric oxide, which kills viruses and bacteria. But



Human cystic fibrosis airway cells infected with a human flu virus.

Listen to the Sound of Your Heart (Pump)

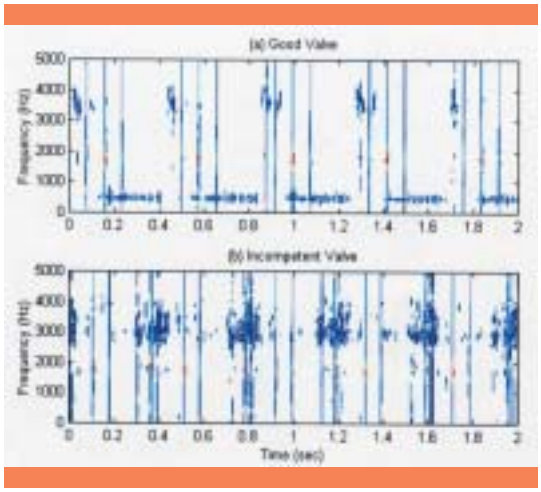
Whether it's an industrial pump, a nuclear submarine pump or a pump that helps a weakened or diseased heart, these pumps all have one thing in common: their components make the same types of sounds.

This finding, established by William A. Smith, D. Eng., of the Cleveland Clinic Lerner Research Institute, and Foster-Miller Technologies (FMT) of Albany, New York, is important because it may help doctors determine if an implanted heart assist pump is beginning to degrade.

"There have been instances where pumps have failed and patients have died," says Dr. Smith. "Surgeons have been frustrated that they were caught unaware of these impending failures. Blood pumps are still new in clinical use and there isn't always a good way to diagnose developing problems with the pump."

Heart assist pumps are used for patients who need a heart transplant. This pump aids the patient's failing heart until a suitable heart donor can be found.

"In the beginning, pumps were only being used for a few weeks, so mechanical wear was not an issue," Dr. Smith says. "Today, more patients are getting pumps for two or three years so mechanical failure can occur." Failure rates are low, but the consequences are very serious.



Acoustic data from a valve in a heart assist pump. The sharp increase in noise (blue lines) between 3,000 to 4,000 Hz can indicate leakage in the bad valve.
Image courtesy of Foster-Miller Technologies

In collaboration with FMT, Dr. Smith is developing a diagnostic tool that is expected to allow doctors to monitor the mechanical performance of a heart assist pump. FMT, considered to be a leading expert in acoustic signature analysis, has developed very sensitive diagnostic tools to monitor performance of pumps at power plants and in nuclear submarines.

"Many industries that use pumps have the same problem we have in the medical field with heart assist pumps; they can't afford to wait until a pump breaks down to fix it," says Dr. Smith. "They have to know weeks or sometimes months in advance that a pump is going bad so that they can be prepared to make repairs or replace the pumps."

Using acoustic signature analysis, experts listen to the components of a pump. Each part makes a different sound. "A ball bearing, for example, has a specific hum and that hum will change before the bearing actually stops working, so an expert can tell when the bearing needs to be replaced," Dr. Smith explains. "We are transferring that technology to heart assist pumps."

FMT is currently developing a prototype clinical instrument that will use very sensitive microphones and sophisticated computer algorithms to break down the sounds transmitted by the pump. By using a mathematical model, acoustic signature analysis will be able to determine if the bearings, motor, valves and other components of the pump are normal or showing signs of wear. This is expected to give doctors data that will warn them whether a pump is failing.

"If we can show that the pump is not operating at its best, that it is on the verge of failing, surgeons can operate and fix it. They could help those patients sooner," says Dr. Smith.

the cells of CF patients fail to make nitric oxide. Dr. Erzurum's research discovered that cells in CF patients do not produce nitric oxide because they don't send out a key host defense gene identified as inducible nitric oxide synthase or iNOS. In addition, the research also showed that CF patients make too much of other molecules, called cytokines, that lead to inflammation of the airways.

"Their bodies can't get rid of viruses quickly and their lungs get overly inflamed because they make too much of the pro-inflammatory molecules," says Dr. Erzurum. "This makes them very, very sick and many CF patients need to be hospitalized with common virus infections."

Because Dr. Erzurum's research indicates why CF patients are susceptible to virus infection, it now may be possible to find therapies that will fortify the lungs' antiviral defenses and prevent infection, which has never been done before with CF patients.

"If we can prevent the viral infection in the first two years of life in CF patients, maybe they wouldn't get bacterial infections until much later in life," says Dr. Erzurum. "By delaying that infection, CF patients may have improved quality and length of life."

THE LONG TRIP

By Shannon Dunn as told to *Cleveland Clinic Magazine*

Last year, when I was in third grade, I started complaining to my mom whenever she hugged me. Every time she squeezed me, my head would hurt over my left eye. My mom took me to the doctor and he gave me some medicine and told us to call back in a week if I didn't feel better.

Then my eye started to swell a little. I didn't like the way it made me look and I didn't want to go to school where the other kids would see it. I didn't feel better, so we went back for a CT [computed tomography] scan. It came back normal. My mom felt a lot better – until I told her my head still hurt. I wondered if I was going to die.

My mom's name is Naomi and she's a nurse. A friend of hers at work told her about The Cleveland Clinic. My mom called and got an appointment the next day. The Clinic is a six-hour drive from where we live in Kenova, West Virginia. We made the long trip to Cleveland that same night; I slept in the backseat the whole time. I was scared, but I didn't care where they took me or what they did – I just wanted to stop hurting.

We went home and a couple of days later Dr. [Joanne] Hilden called my mom with good news. They told me the tumor was caused by Langerhans Cell Histiocytosis. It's a big name, but what it means is that my body sometimes makes too many of a type of white blood cell, the kind of cell that's supposed to fight infection. These cells all clump together in certain areas and cause problems. They told me that I'd be fine after taking medication to get rid of my tumor.

After that, my dad drove us on the long trip back and forth to the Clinic every Friday for 12 weeks in a row for my chemotherapy.

My aunt had quilted this great bag out of purple material, my "Cleveland Bag," and inside it I usually brought a doll named Sarah that I've had since I was a year old and other things like crocheting and coloring books and videos. My friends at school all signed their names on a pillowcase and I brought that with me, too.

Left to right: Naomi Dunn and Holly Kubaney, A.P.R.N.; art by Shannon Dunn; Shannon Dunn

The Clinic is huge but the nurses and other people there were really, really nice. They did a lot of blood tests, X-rays and an MRI [magnetic resonance imaging]. After each test I got to pick out a toy from a chest full of prizes. That day I got a lot of toys; I really liked the hair clips best.

The doctors told me that I had a tumor in my left temple and that I'd have to have surgery. The night before the surgery, Tom [Richards] from the hospital gave me a tour of everything. The next morning he met us in the surgery area and gave me some crayons and some pictures of the operating room so I wouldn't be afraid of where I was going next. Dr. [Julian] Perry did my operation. He took out a piece of the tumor so the doctors could figure out exactly what was wrong. You can hardly see my scar.

On one trip to Cleveland, I brought a stuffed animal named Mr. George with me. I had to do a school report about everywhere we went that weekend. They took an X-ray of Mr. George and I took a picture of him and his X-ray for my report. I drew a map of the route Mr. George took on the way to Cleveland. I also took pictures of the nurses examining Mr. George. My report was good and I got an A.

It's been a year since my last chemotherapy. I am now ten years old and completely better. We keep going back to the Clinic for check-ups, which I kind of look forward to. I made friends with some of the other kids there and I like saying hello to all the people who helped me. It feels familiar when I go back and, best of all, I don't feel sick anymore. I tell other kids that I got medicine at the Clinic and it helped.

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