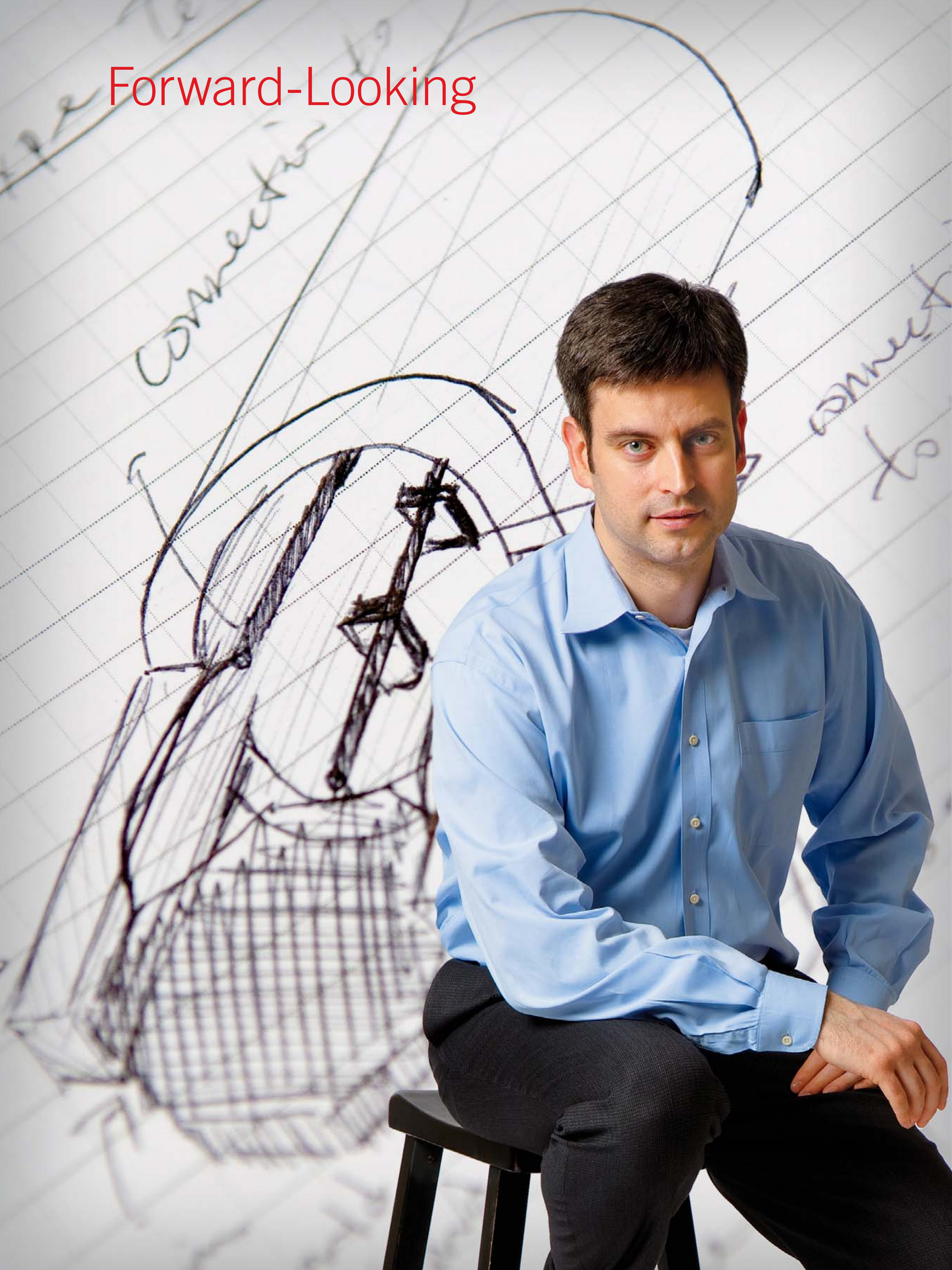
Forward-Looking



The heart is a powerful and much-studied organ. The ability to visualize the workings of its chambers and vessels remains a challenge, however, a serious obstacle given that most of what goes wrong with the heart—including cardiovascular disease, the primary cause of death globally—happens there. Needed is a better way to see what goes on in these innermost places. One Sunnybrook trainee may have found it

By Stephanie Roberts

On cinema screens across North America, 3-D is hotter than ever. The fantastical concepts of *Avatar* and *Up* exist, however, in the realm of the imaginary. Not so the ideas of one enterprising clinician-researcher at Sunnybrook Health Sciences Centre, who has also harnessed the power of 3-D, but in the sphere of the real. Dr. Brian Courtney has built a device that can see inside the heart's chambers in three dimensions—no geeky plastic glasses required.

His invention takes aim at some of the stickiest challenges facing 21st-century cardiology. "When we're talking about complicated procedures like burning or ablating structures in the heart to get rid of a heart rhythm problem, or putting in new devices, like a replacement valve, then it becomes a three-dimensional problem, and there aren't very good techniques to guide these 3-D procedures at this point," says Courtney.

Rather, there weren't.

Courtney's device builds on a technique called intravascular ultrasound imaging, IVUS for short, which is done in about 15% of patients in North America who have a coronary angioplasty or stenting procedure to open blocked blood vessels. The technique is used to ensure stents have been placed correctly, or to identify things that a coronary angiogram, a type of X-ray that is the workhorse of the cardiac cath lab, cannot see.

During IVUS, a catheter, a thin tube, is threaded from an artery in the leg or arm into a blood vessel in the heart. At the catheter's tip is an ultrasound transducer, or probe, which looks off to the side. It sends the information it captures back to an ultrasound machine for viewing. In this way, clinicians can see inside a blood vessel and be confident in doing procedures like angioplasty that the stent they've chosen is the right size and properly positioned.

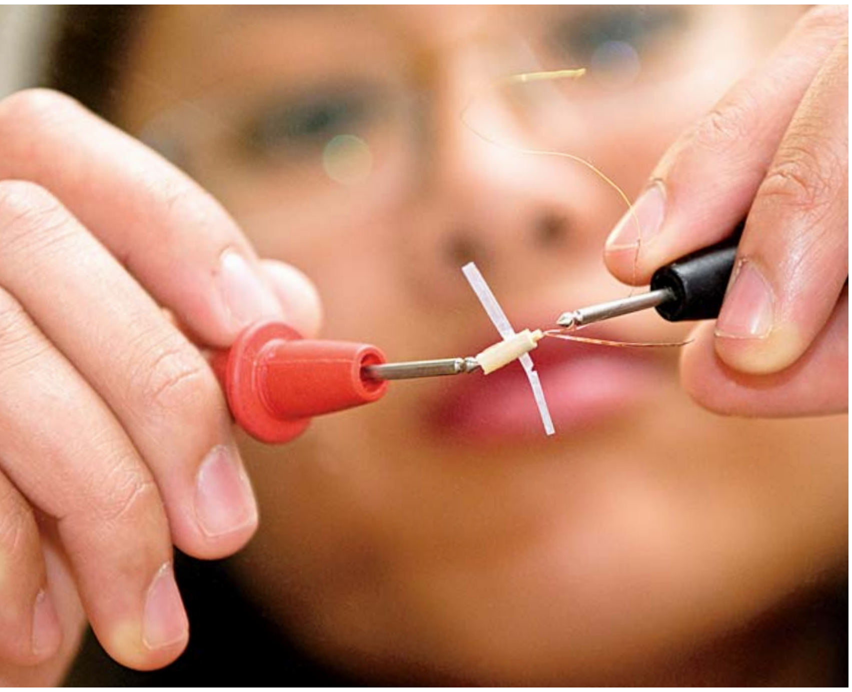
While IVUS catheters take pictures of vessels, a larger version, called an intracardiac echocardiography (ICE) catheter, takes pictures of bigger structures and chambers. Both types of catheters, IVUS and ICE, however, are limited to 2-D imaging. Moreover, as cardiovascular procedures become more complex, patients are exposed to a lot of radiation or kidney-damaging dye.

Courtney's coolly named 3-D forward-looking ICE catheter solves these problems by displaying images in high-resolution 3-D in real-time. And, it offers another inventive twist: the capacity to look ahead of its tip, instead of only to the side. "When I explained it to my mother, she said, 'Oh, so current catheters are like driving but looking out the side window, and forward-looking catheters are like looking out the windshield, so you can actually see where the car is going,'" says the 36-year-old, smiling. "I've used the analogy ever since."

A PROGRESSIVE SPIN

With these capabilities, clinicians can get the catheter closer to the tissue of interest. It also can reduce the need for X-rays and helps with navigation, says Courtney: "If you have a forward-looking

DR. BRIAN COURTNEY



device, then you can see ahead of the device, and you can see where you are moving the catheter toward."

The innovation is a feat others have tried to own. "People have been working on this for 20 years—to come up with a catheter that is forward-looking using ultrasound imaging," says Courtney. "They've struggled with it because these catheters have to be disposable, therefore they have to be somewhat inexpensive, they have to be reliable and they have to produce good images."

Where others have failed, Courtney and his team at Sunnybrook Research Institute (SRI) are succeeding: they've shrunk it to be the same size as a 2-D ICE catheter, and the images they've made with the prototype were very good: "better than we were expecting," he says.

Price-wise, he estimates his 3-D forward-looking ICE catheter will ring in at less than one-half of the $3,500 it costs in Canada for the 2-D version. New technologies, especially advanced ones, aren't known to come in cheaper at the outset, so how is this possible?

To understand how, one need take a step back, to learn a bit about how ultrasound catheters work. At the tip of a catheter is a transducer, an electrical device that converts one form of energy to another, in this case, sound waves to electrical signals. Inside the catheter is a torque cable that is attached to a motor. Images are produced when the cable is rotated, typically at about 30 rotations per second, causing the probe to look out, spin around and capture information. This information is received by the ultrasound machine, which processes the signals to produce an image on a monitor. Advanced 2-D catheters have probes composed of many electronic elements, which helps with resolution but makes the technology much more expensive.

Courtney's approach is different: "What we do is take a single element or a single transducer, and just change the direction of the rotation using a mechanical concept.

"We mount the catheter on a pivot point and change the speed of rotation. When we go at slow speeds our catheter looks off to the side; but when we really spin the torque cable, the transducer, which is at the far end of that cable, is mounted in such a way that centrifugal force causes it to tilt. So at very high speeds it looks forward." Relying on mechanics rather than electronics makes it cheaper to build and thus to buy.

AN ENTERPRISING MIND

So, the 3-D forward-looking ICE catheter hits the mark on novelty, image quality and cost-effectiveness. Results from the ultimate test, however—impact on patient care and by extension the health care system—won't be seen until the device is in doctors' hands, some years away.

To get there faster, Courtney has founded a company to commercialize the technology. Colibri, Latin for hummingbird ("They are fast, efficient and beautiful," he explains), was incorporated in November 2007. Courtney is its president and CEO. He and six co-founders wrote the original patents.

The initial focus of Colibri is the described 3-D image-guidance technology, a broad-based imaging platform with many potential applications. Courtney is also building a device that could have even bigger impact: a catheter that can detect a heart-attack-in-the-making.

At the core is "vulnerable plaque," a type of fatty buildup that forms in the wall of an artery. This lipid-rich plaque stays hidden in the wall, sheathed by a thin coating, until something causes it to rupture—high blood pressure or inflammation, say. When it bursts, the plaque leaks into the artery and causes a clot to form. The clot strangles blood flow, which brings on a heart attack or stroke, and not infrequently, sudden, shocking death.

Often, victims of a detonated vulnerable plaque have no idea they're in peril until they're stricken. Most pressing, then, is a means to identify these plaque before it's too late. Current technology doesn't have the power to do this.

Courtney's might, though. It would be able to detect if the cap covering a fat-filled plaque has thinned, one sign of a lurking vulnerable plaque and often a precursor to a heart attack. It could also identify plaque with a lipid-rich centre, another indicator. To do this, Courtney has coupled ultrasound and optical imaging, creating an innovative tool that is greater than the sum of its parts.

WEDDED BLISS

Ultrasound is good at seeing through blood and relatively far through tissue, two tasks that defeat optical imaging. Where optical imaging triumphs, however, is in its high resolution and contrast, capabilities ultrasound lacks and that give doctors the sensitivity and specificity they need to distinguish a nonthreatening from a potentially fatal plaque.

"If you were to look at a plaque that was filled with scar [tissue] but that doesn't have a lot of lipids in it, then that's a plaque that's probably less dangerous than one that has a lot of cholesterol deposits and a thin fibrous cap over it. Optical coherence tomography is able to identify whether there is a lipid- or cholesterol-rich core to a plaque. It's also able to identify a thrombus [clot] in a blood vessel better than ultrasound or angiography."

Courtney's catheter is the first to marry the two technologies to produce an all-in-one imaging capability. "We built it in such a way that the ultrasound and optical imaging are precisely coregistered with each other, so when you take an ultrasound image and you take an optical image, you know that you've taken each of the exact same place in the blood vessel, and you can map the two information sources on top of each other, so you can take advantage of each of them," he says.

As a third-year resident in the department of cardiology at the University of Toronto (his research and much of his clinical training are at Sunnybrook), Courtney has been able to gain

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insight into patients' needs, as well as those of his physician peers. "The clinical community has been very supportive. I get to talk to a lot of doctors that do procedures that would potentially benefit from this kind of technology."

Indeed, at every step of the way, the trainee has garnered the interest of colleagues in medicine and research. "We've probably shown our idea to people who together have hundreds of person-years of experience in the field, and everyone has said, 'That's very interesting. I've never seen anything like that before.'"

SPLIT PERSONALITY

Courtney's multi-branched focus is atypical. Rare is a doctor who is a researcher who is an entrepreneur.

Colibri is his third start-up company, the last two being in the U.S. while he was attending medical school at Stanford University. This is the one with which he has been most involved, he says. The benefits to patients are clear, and there is a bona fide business opportunity. "We can help a lot of people. It makes it easy to tell the same story to the clinicians as you tell to the business people," he says.

His dual focus on medicine and research seems a natural fit. He says he is motivated to do science because he wants to do better medicine. "I enjoy looking after patients and the complexities of day-to-day clinical medicine," he says. "But there are situations that we see routinely that are limited by the tools we have available, where patients suffer or we spend way too much money. I think there are many ways of doing things better."

BRIAN LI, DR. BRIAN COURTNEY, ANNIE LEUNG AND ALAN SOONG

Being on the frontline of care is as crucial, he says: "If I were to be a researcher or entrepreneur all the time, I'd be frustrated because I wouldn't get the day-to-day joy, the sense of doing things for patients and seeing the result, and I'd be farther removed from the context of why I'm doing the development."

He credits the milieu at SRI as instrumental in deciding where to do his residency. "Here, we're able to build not only ultrasound systems from the ground up, but optical systems from the ground up. There is technical expertise here that enables us to be very flexible in our design, well beyond what most other imaging research centres in the world can do."

There are the top-tier facilities at SRI; there is also the highly rated imaging research team. He cites in particular the mentorship of senior imaging scientists Drs. Stuart Foster and Graham Wright, both world-renowned in their respective fields. He's working with Wright and Dr. Brad Strauss, a clinician-scientist in the Schulich heart research program, on using his 3-D ICE catheter to provide image guidance during a range of cardiovascular procedures.

Longer-term, Courtney says the focus may turn to therapy. "Once we build a catheter that can do the imaging to help guide procedures, it might be worthwhile to combine some therapeutic capabilities onto these catheters. Then we would be able to build things that would combine therapy and 3-D image guidance on the same catheter," he says.

That'd be another first.

Today, though, the focus is on technology development—refining, validating and testing the device, which includes securing more funding to accelerate activity. Rarely easy, the economic climate has made it even more challenging, though Courtney notes there has been an "up" side. "It meant that we really had to focus and be efficient. The best ideas that come out of a time where funding is this difficult to get means that only the best ideas will survive. I am hopeful that we have a very good chance of being one of the success stories."

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