Interventional cardiology, where doctors use catheters to open narrowed arteries of the heart, is the gold standard of care for patients with heart disease. To be successful, doctors have to be able to see where they're going, a tough task in the case of stubbornly clogged blood vessels. To beat this problem, a scientist has invented a device that enables doctors to visualize previously invisible corridors of the heart BY ALISA KIM

DR. CHARLES CUNNINGHAM; PHOTOGRAPHY: CURTIS LANTINGA

Computer scientist and visual artist John Maeda, widely known for his book *Laws of Simplicity*, argues that "thoughtful reduction" and the skilled application of knowledge are ways to enhance design. Maeda, a technology and design expert, points to the iPod's spare gadgetry as an example of the kind of elegance and functionality that can be achieved through simple, yet carefully considered design. Of the computer giant, Maeda has said, "Apple products aren't simple technologies by any stretch, but there is a beautiful simplicity to them."[1]

Dr. Charles Cunningham, a physicist in the Schulich Heart Research Program at Sunnybrook Research Institute (SRI), has invented a medical device with a simple design to tackle a complex health issue. Over the last four years, Cunningham has developed a technology for use in the treatment of blocked coronary arteries, the most common form of heart disease in the western world.

The heart is the body's most important muscle. Always at work, it moves over 11,000 litres of oxygen- and nutrient-rich blood around the body each day. Vital to this circulation are healthy coronary arteries. As we age, lipids floating in the bloodstream, coupled with an inflammatory process, can form a plaque that protrudes from the inner walls of the blood vessels. The buildup of this plaque restricts blood flow to the heart. A coronary artery that is completely blocked for longer than three months is called a chronic total occlusion (CTO).

Cunningham's device was designed to improve the success rate of CTO crossings, a procedure in which interventional cardiologists open a narrowed artery by passing a guide wire with an empty balloon at its tip (a balloon catheter) through the middle of the months-old blockage. The guide wire is inserted through a needle puncture made in the upper thigh. Under X-ray guidance, the wire is snaked through the passageway of the affected vessel, into the blockage, where the balloon is inflated to crush the plaque and restore blood flow. Although a CTO crossing is preferable to coronary bypass surgery, because the latter requires hospitalization and longer recovery, it accounts for just 10% of all percutaneous or through-the-skin cardiac treatments.

The main reason that CTO crossings fail is cardiologists' inability to pass the guide wire through the occlusion, a function of the limitations of current imaging practices. The procedure is normally done via X-ray angiography, through which images are obtained using a fluoroscope and an X-ray dye that is injected in the patient's artery to highlight it on X-ray images. In a patient with a CTO, the flow of the dye stops at the blockage, which prevents clinicians from seeing the wire and the vessel past the occlusion—crucial information if they are to perform the procedure safely and effectively.

DR. WILLIAM DOMINGUEZ-VIQUEIRA AND DR. CHARLES CUNNINGHAM

Magnetic resonance imaging (MRI) overcomes this constraint by providing contrast between the blocked part of the vessel and the surrounding tissue, without any dye. "That's the big advantage of MRI: being able to see the path of the occluded vessel, the device and the open vessel all at the same time," says Cunningham, who is also a professor in the department of medical biophysics at the University of Toronto.

The CTO crossing can also be troublesome because many plaque deposits have a hard, fibrous "cap" covering the first segment of the blockage, making the lesion harder to penetrate. Further, while angiography provides images of the open part of the vessel in real-time, MRI reveals the plaque's structure, including calcifications and softer, lipid-rich areas that are easier to treat. Cardiologists need adequate depiction of the vessel wall boundaries and the make-up of the lesion to figure out the proper path of the wire to avoid puncturing the artery.

Electronic tracking devices that work well with MRI can be built, but pose safety risks if used inside patients while they are in the scanner. Moreover, such devices are complex and expensive to manufacture, an unviable option given that in this setting they would be used just once. Needed is a safer and cheaper way to locate the position of a device using MRI during coronary diagnoses and treatments.

Enter Cunningham's catheter tip.

"What our device gives is position and orientation information—how the device is positioned against the occlusion. It will enable visualization of the part of the occlusion where the dye won't go. We're hoping [the interventional cardiologists] will wheel the patient into the MRI scanner and for that step, where they push through the first part of the occlusion—the hard-to-cross part—that it can be done under MRI guidance using our device," he says.

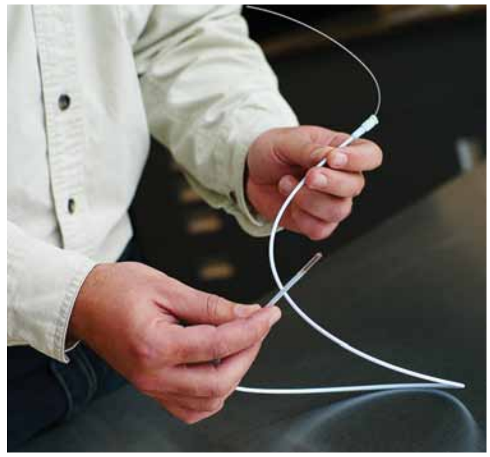
Part of Cunningham's lab is housed within SRI's Imaging Research Centre for Cardiac Intervention, a state-of-the-art facility that contains an integrated X-ray and MRI suite—an appropriate setting for the creation of this device. The technology evolved out of his interest in magnetic susceptibility, the tendency of a material to become magnetized in response to a magnetic field. In particular, he was intrigued by the way in which devices with magnetic material can be detected through the "dark spot" they create in the MRI scan. This dark spot, created by the magnetic-field disturbance from the device, is what's known as an artefact—something that appears in the image, but that doesn't exist in the object itself. The artefacts from devices can be useful in that the dark spots they produce on MR images allow devices to be tracked. Artefacts are also problematic, however, because they prevent images from being taken at the device's tip.

The beauty of Cunningham's catheter tip is that it allows the user to control the appearance of artefacts.

"Say you're looking at the plaque in the artery. You can't image right by the tip [of the catheter] because the artefact is so big," says Dr. William Dominguez-Viqueira, a research associate in Cunningham's lab who helped develop the device. "With this, you can produce a big artefact just to see where you are, then change the position of the device to remove the artefact to do images right at the tip."

The design of the device is clean and minimal. About three centimetres long and only three millimetres in diameter, it is shorter than a standard paperclip, but resembles a much smaller and lighter triple A battery. The device attaches to the end of a catheter and consists of an outer titanium layer, a middle graphite layer and a titanium wire on the inside. Cunningham used these materials because in addition to being inexpensive and plentiful, they have roughly equal and opposite magnetic properties.

Titanium is paramagnetic: it has a positive magnetic susceptibility and is slightly attracted by a magnetic field. Graphite is diamagnetic: it has a negative magnetic susceptibility and is slightly repelled by a magnetic field. In the "off" position, the parts are aligned and the magnetic fields of the materials cancel out one another. A minimal artefact appears on the image, allowing the user to see what is at the tip of the catheter. When the graphite layer within the device is moved using a wire running down the catheter, the effect from the device is "turned on." The resulting magnetic disturbance produces artefacts at both



In particular, he was intrigued by the way in which devices with magnetic material can be detected through the "dark spot" they create in the MRI scan.

ends of the device, allowing the interventional cardiologist to see the exact position of the device and its orientation relative to the occlusion on the MR image.

Cunningham used computer models to study the magnetic fields created by differently shaped parts and how they would work together, which streamlined the design process. "We were able to figure out the thicknesses and geometry of the device in a computer model and use that to have the pieces manufactured. Otherwise you'd have to try and make the device with a whole bunch of test thicknesses and test them all to see which one was better. We did all of that in the computer and just made the one device that worked," he says.

Building the first tip was fairly straightforward. "We made this in a conventional machine shop using a lathe and drill, to drill out the centre," says Cunningham, holding up a clear container with the first prototype suspended in water, to simulate the inside of a blood vessel. "We did the experiment where we had this in the MRI scanner moving the pieces and seeing the effects come and go. We got to that step pretty quickly."

Shrinking it to fit onto a catheter, however, proved to be more challenging. "We began with a really big tip. This was to prove that the materials work. To do the machining for this tiny thing is not easy," says Dominguez-Viqueira, who worked on miniaturizing the device.

He and Cunningham spent a lot of time sussing out a manufacturing facility that could make the components to the appropriate size and thickness. They had to send the parts to a plant in the U.S. that does microelectrical discharge machining, a specialized technique for drilling tiny holes using high-voltage sparks. They are now able to build prototypes more efficiently at SRI, with the recent opening of the device development lab that is part of the research institute's Centre for Research in Image-Guided Therapeutics. "In terms of prototyping, we'll definitely do it here because even if we license it, we'll have something to show that works—something that's the right size and the right feeling for cardiologists to actually use," says Cunningham.

With the scientific research for the project completed, more funding is needed to move the technology further along the innovation pipeline. In the months ahead, Cunningham plans to build a large number of prototypes to send to cardiologists for evaluation. He and Dominguez-Viqueira have already filed an international patent for the device; they now need to decide in which countries they will do national patent applications, which cost about $10,000 each.

Cunningham has partnered with MaRS Innovation, an organization that works with SRI and other Toronto-area research institutes to commercialize promising discoveries. Dr. Fazila Seker is a project manager at MaRS Innovation who is working with Cunningham to advance this process. While researchers look at their breakthroughs from a scientific viewpoint, MaRS Innovation looks at technologies strategically, with a view to translating them into marketable products and services.

Cunningham and Dominguez-Viqueira, along with Seker and other staff from MaRS Innovation, comprise the "deal team." Together, they will decide what the next step will be, whether it is meeting with companies who may be interested in licensing the technology or forming a startup company. "If it's decided that a startup is the way to go, [then] the next step is to raise capital and start looking at hiring the right type of expertise," says Seker.

She says that MaRS Innovation offered its product management and business development services to Cunningham because the technology shows commercial potential. "The device is unique in that it looks at the interventional MRI market opportunity. That's really the way of the future when it comes to imaging. There aren't a lot of devices on the market that would work well with MRI so it's very much a development area," she says.

The technology has been developed as a standalone catheter, but the magnetic tip of the device can be integrated into existing catheters. It is ready for preclinical testing. In addition to making more prototypes to give to cardiologists, Cunningham must obtain government approval to use the device in clinical trials, all of which could take a few more years. Like Seker, he believes MRI research is a field in which there is room for innovation. "Research on devices for use inside the MRI scanner is a really fascinating area that, I think, has yet to reach its potential. Catheters that are available commercially would be a big step forward. That's what we're trying to do: make devices that work and can be sold for a reasonable price."

Cunningham's research on catheters is funded by the Canada Foundation for Innovation, Canadian Institutes of Health Research and Ontario Ministry of Economic Development and Innovation.

1. John Maeda, "Why Apple Leads the Way in Design," *Huffington Post*, http://www.huffingtonpost.com/john-maeda/technology-design-apple_b_291748.html