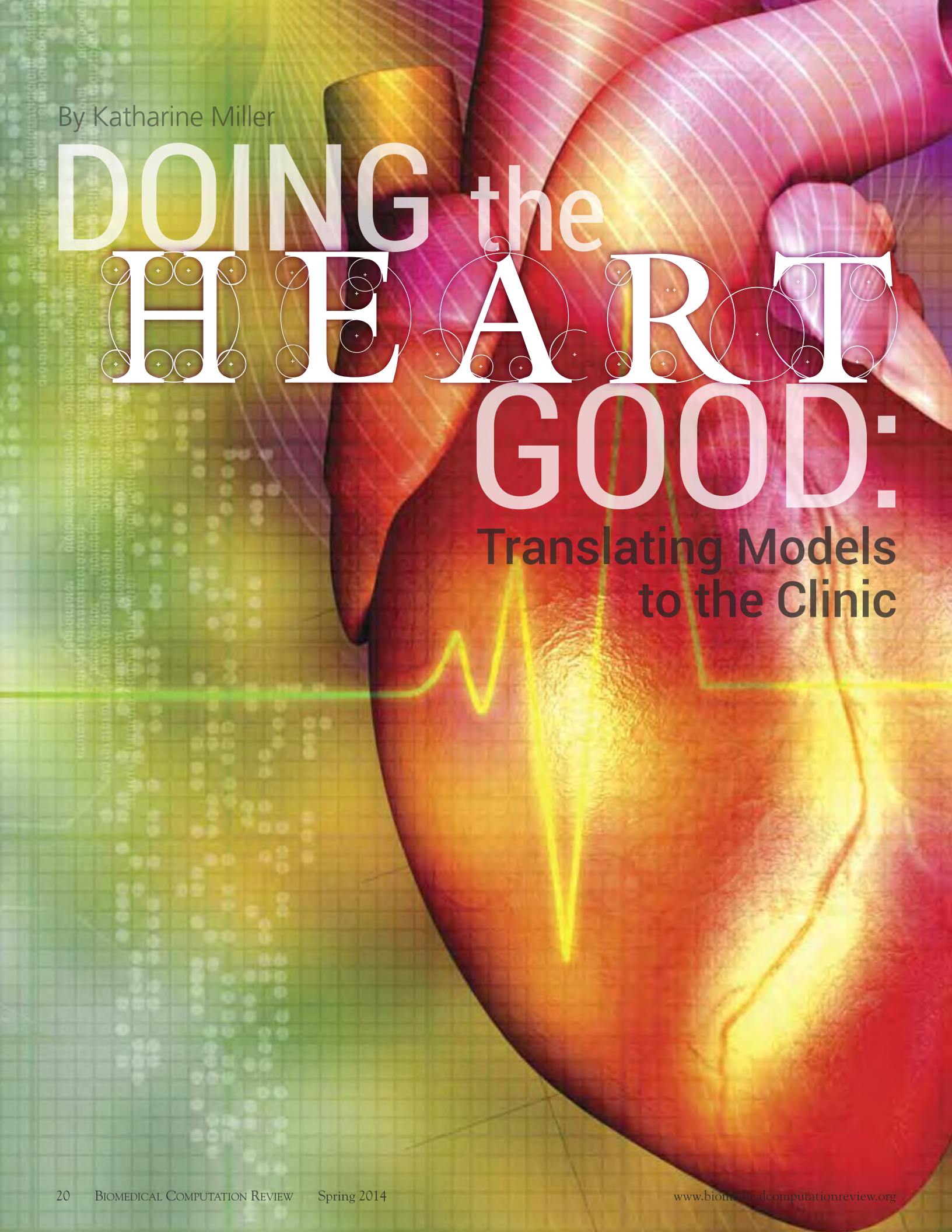


By Katharine Miller

DOING the HEART GOOD:

Translating Models to the Clinic

Pacemakers, heart-lung machines, stents and artificial hearts all sprang from successful partnerships between engineers and doctors. "From its inception in the 1950s, heart surgery has motivated advances in engineering technology, and engineering technology has enabled advances in medical treatment," says **Alison Marsden, PhD**, associate professor of mechanical and aerospace engineering at the University of California, San Diego. "I personally view modeling and simulation as the next step in this long history."

Modeling and simulation have the potential to help physicians answer some of the most fundamental clinical questions: Who is at risk if not treated? Who will benefit from treatment? And what is the best treatment for the patient in front of me?

Such clinical applications will only succeed if modelers and clinicians work closely together, says **Tain-Yen Hsia, MD**, a consultant cardiothoracic surgeon at Great Ormond Street Hospital in London, UK, who has collaborated with Marsden on modeling projects. Engineers need to educate physicians and surgeons about the potential and limitations of modeling. Clinicians, in turn, must educate engineers about the most clinically relevant questions and problems, he says.

Currently, only a few cardiovascular mod-

eling efforts are sufficiently lightweight for actual use in the clinic, but that is rapidly changing. And there is one sad fact that works in modelers' favor: Too many people are either being overtreated or undertreated because doctors don't have enough information to accurately predict risks and outcomes. Models have the potential to change that—and they only have to do better than current practice, a lower bar than one would think.

WHO IS AT RISK IF NOT TREATED?

Modeling and simulation can be used to noninvasively stratify patients' risk of various cardiovascular conditions (such as heart attack, arrhythmia, atherosclerosis, or blood clots). This can help to reduce overtreatment of lower-risk patients and undertreatment of higher risk patients, Marsden says.

Modeling Heart Disease Risk

One company, HeartFlow, Inc., seems to have hit the sweet spot. Their service seeks to improve how clinicians assess a person's risk of heart disease due to reduced blood flow in the coronary artery. Currently, the process often goes like this: If imaging shows more than 50 percent narrowing of the coronary artery (a condition known as stenosis), cardiologists send patients to the cardiac catheterization lab (cath lab) to have a stent implanted. Evidence suggests, however, that anatomical narrowing is not a good proxy for reduced blood flow, says **Charles Taylor, PhD**, founder and chief technology officer at Heartflow. A better measure is called the fractional flow reserve (FFR). Here's how it works: In the cath lab, the interventional cardiologist administers a drug to make the heart pump as it would under exercise; inserts a wire into the artery to measure the blood flow upstream and downstream of the narrowed region; and calculates the ratio between these flows—the FFR. An FFR of less than 0.8 indicates reduced function and the need for a stent or other procedure to widen the artery.

It turns out, though, that only about 20 percent of patients who are sent to the cath lab with coronary artery narrowing have greater than 50 percent diameter reduction, according to a recent study published in the *Journal of the American College of Cardiology* (JACC) in 2012. Many of these lesions won't be functionally significant. In other words, 80 percent of patients who go to the cath lab for stenting or FFR assessment—expensive procedures that carry risks of their own—don't need to be there, Taylor says. "The artery may be anatomically narrowed but it may not really matter in that specific patient."

This is where HeartFlow comes in. Using CT images from individual patients, Taylor and his team can simulate blood flowing through the coronary artery under exercise conditions and then calculate the FFR noninvasively. In a recent study of 254 patients, this personalized modeling approach, termed FFR_{CT}, proved capable of reclassifying 68 percent of the false positives as negative. "FFR_{CT} may spare many patients a trip to the cath lab," Taylor says. The work was published in January 2014 in the *JACC*.

HeartFlow's technology is approved for use in Europe and is currently waiting for FDA clearance in the United States. Taylor notes that HeartFlow's product is unusual because it doesn't try to predict an outcome. "We just need to show how good our measurement is," he says. So far, Taylor is quite confident that the procedure is better than the current protocol, which is dominated by what many cardiologists jokingly call the "occulo-stenotic reflex": See stenosis and treat it.

> Heartflow seems to have hit the sweet spot with a service that seeks to improve how clinicians assess heart disease risk due to reduced blood flow in the coronary artery.

Modeling the Risk of Losing Heart Rhythm

Natalia Trayanova, PhD, the Murray B. Sachs professor of biomedical engineering and medicine at Johns Hopkins University and Chief Scientific Officer at Cardiosolv LLC, is developing patient-specific computer heart models to predict which patients are at risk of dangerous arrhythmias—ventricular tachycardia [VT] or ventricular fibrillation [VF]—due to scarring from a heart attack.

Currently, to assess the risk of VT or VF, cardiologists measure a heart attack patient's left ventricular ejection fraction—the percentage of blood in the ventricle that is pumped out with each heartbeat. If a patient's ejection fraction is less than 35 percent (normal is 55 to 70 percent), the physician implants an ICD (implantable cardioverter defibrillator), a special kind of pacemaker that automatically detects heart rhythm and applies a shock to bring the heart back into rhythm. Yet, annually, fewer than five percent of these implanted ICDs ever have to fire to terminate an arrhythmia, Trayanova says. Thus, many people who were implanted don't need the device; and on the flip side, some heart attack patients with ejection fractions greater than 35 percent—who don't receive the device—need it, she says.

Trayanova wants to see if modeling can do a better job of predicting who is actually at risk of a dangerous arrhythmia. To that end, her team has simulated electrical activity in 40 patient-specific heart models of people who have ICDs. The result: In cases where the model predicted no arrhythmia, the devices have never fired.

The team still has to determine the minimal set of simulations that will be optimal for determining risk and to streamline the process. But, she notes, "We just have to do better than the current protocol." And since the protocol leads to the costly implantation of ICDs in patients who don't need them and non-implantation in people who do need them, Trayanova's models have the potential to improve patient care while also reducing costs.

Modeling the Risk of a Clog

The Heartflow FFR_{CT} protocol evaluates impaired coronary flow reserve at the time of examination. It does not, however, attempt to predict the future—for example, whether a patient is likely to develop atherosclerosis—a condition in which the walls of the arteries thicken and harden with plaques. The ability to predict the progression of plaque would be extremely useful for determining who should receive medical treatments such as statins.

Currently, physicians review MRI or CT scans and blood test results to try to infer

Translating Models to the Clinic:

Advice to Engineers

Collaborate deeply.

It used to be that clinicians were deeply skeptical of working with computer modelers. That was at least in part because modelers tended to solve the most numerically interesting problems rather than those with the greatest potential impact on medicine, Marsden says. But these days, "Getting collaborators is usually the easy part," she says. "The challenge is narrowing down the key clinical questions we can contribute to effectively." To do that, she says, engineers cannot work in isolation. "You have to have constant interaction with the clinical team so you can improve the model, incorporate new data, and change the question as you start to get answers."

Keep it clinical.

"One of our translation goals is to get the models to produce quantities the clinicians are familiar and comfortable with," Marsden says. Her computational fluid dynamics (CFD) models provide information on local hemodynamics and energy loss—terms rarely used by physicians. So she wants to couple the CFD models to physiological models that will allow calculation of measurements of greater interest to clinicians, such as oxygen saturation, pressure loss, or cardiac workload.

Similarly, Trayanova notes that if a model can reproduce quantities with which clinicians are familiar—electrocardiogram results, for example—"then they are more likely to believe."

Make it cost-effective.

Economic modeling of the cost-effectiveness of FFR_{CT} suggested that it would save money while having no adverse impact on patient outcomes—and perhaps even having a positive one. The work was published in *Clinical Cardiology* in 2013. In a multisite study, Heartflow is now comparing the economic and clinical outcomes of patients evaluated with either FFR_{CT} or the current standard of care. Taylor believes that the results will also show cost savings with no adverse outcomes. By doing better than the current protocol—and doing it efficiently and noninvasively—Heartflow has received positive feedback from many health insurance providers, Taylor says.

Remember the FDA.

A critical and sometimes challenging part of any effort to bring models to the clinic is the need for FDA approval or clearance. Heartflow is currently waiting to hear back from the FDA on its application for clearance to sell its service, at which point the company should become eligible for insurance reimbursement.

For some models, it's unclear whether FDA review will be necessary. For example, Marsden's Y-graft for the Fontan procedure wouldn't require FDA approval if seen as a surgical procedure (because a surgeon is free to implement whatever design s/he thinks is best for the patient), but would require approval if deemed a device. "The Y-graft involves sewing together a trunk with two branches. Whether that's a device or surgical method is perhaps fuzzy," she says. It gets even fuzzier if the grafts are made patient-specific (which Marsden believes would improve outcomes).

The FDA is also still figuring out exactly what data they will require to demonstrate that a simulation tool is sufficiently reliable for clinical use. They will likely want to see an error bar or confidence interval before deciding if something is safe for the clinic, Marsden says. So modelers need to start doing uncertainty analyses. "Clinical data is full of uncertainty, and you need to know the uncertainties of the input and how those propagate through to the model output." Since uncertainty quantification is a field unto itself, Marsden advises teaming up with people with that expertise.

Make it lightweight.

"There's always a tension between doing things that are cool and doing things that are practical," says **Hiroshi Ashikaga**, **MD**, **PhD**, assistant professor of medicine and biomedical engineering at Johns Hopkins University. "But the ultimate test is whether clinicians would like to use a model." Portability and simplicity are key. "Clinicians want to get things done." So modelers should try to develop portable systems where all the clinician has to do is download images, put it in the model, and get the results, he says.

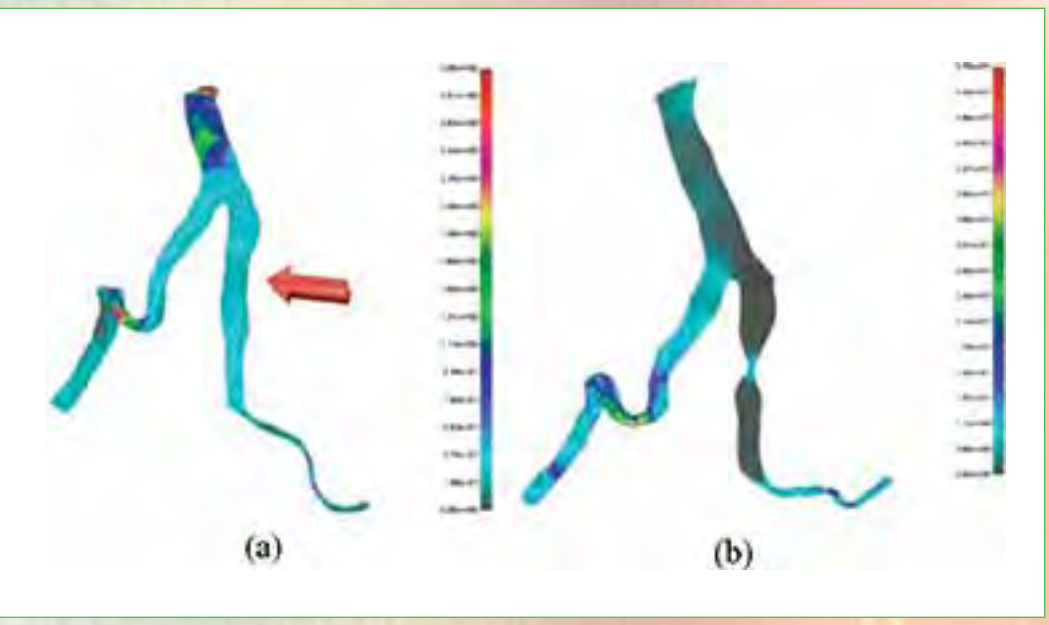
To reduce computational times, researchers are trying time-saving computational approaches, such

how a patient's clogged arteries will evolve: Will they get more clogged or stay the same? And how fast will they change? "Despite being an experienced clinician, I couldn't do this in my head," says **Oberdan Parodi, MD**, a cardiologist at the Ospedale Niguarda Ca' Granda in Milan, Italy.

So Parodi collaborated with researchers who were part of Europe's Virtual Physiological Human project ARTreat to develop a multi-scale computer model of plaque formation and evolution. It combines 3-D image reconstruction of the arteries with blood-flow modeling and models of the initiation and progression of plaque, as well as plaque characterization.

Parodi's model considers the transport and chemical interaction of LDL and HDL; the role of adhesion molecules; the movement of cells and other materials in the bloodstream; and arterial wall thickening. In the end, the model calculates wall shear stress—the forces exerted on the arterial walls—using computational flow dynamics. And by calculating it at multiple points along the artery wall, Parodi can detect the locations where plaque will likely form. "That's relevant from a prognostic point of view for managing this patient," he says.

Parodi validated his model in pigs (who could be sacrificed) but thus far has only been able to test the model in 64 relatively healthy human patients who had less than 50 percent plaque blockage (patients with major blockages need to be treated immediately). "We were able to see several plaques that progressed as well as the new onset of plaques over time and in places the model predicted," Parodi says. More human studies are needed, he says. "This model is still a prototype. Getting it into the clinic requires more testing and money."



Parodi modeled plaque progression in the coronary arteries of 40 patients over the course of two years. The colors indicate arterial wall stress, with gray representing low stress. Here, the models observed an increase in plaque and a narrowing of the vessel after six months (b) at the original site of lowest wall stress (red arrow in (a)). Reprinted with permission from Parodi, O,* et al.*, Patient-Specific Prediction of Coronary Plaque Growth from CTA Angiography: A Multiscale Model for Plaque Formation and Progression,* IEEE Transactions on Information Technology in Biomedicine *(2012).

WHO WILL BENEFIT FROM TREATMENT?

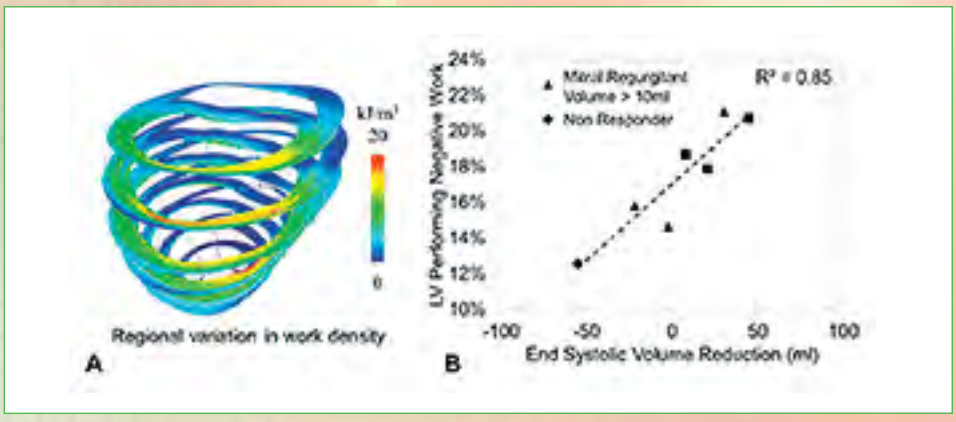
Some models go a step further than the models described above: They simulate a possible treatment and try to predict the outcome. The goal is the same—to identify which patients will likely benefit from treatment—but the models simulate treatments in addition to patient physiology.

Modeling Who to Pace

About 40 percent of patients with heart failure suffer from a double whammy: They have defects in both electrical conduction and pumping. "Their contractions are not only weaker, but also less synchronous," says **Andrew McCulloch, PhD**, professor of bioengineering at UCSD. These patients are typically implanted with two pacemaker leads—one on each ventricle—to resynchronize the contractions between the left and right sides of the heart. When this cardiac resynchronization therapy (CRT) works, it improves the mechanical function of the heart.

For unknown reasons, CRT fails about one-third of the time. But McCulloch's team may be the first to be able to predict when this will happen. Using patient-specific modeling in eight patients, his team found a nearly linear correlation between successful CRT and a calculable quantity called "heterogeneity of regional work." Essentially, CRT is most beneficial when the distribution of work across the heart muscle is not uniform.

McCulloch's team plans to test the model in more patients. But here's the catch for translating this model to the clinic: You can't measure regional work directly; you have to calculate it based on detailed measurements—some of which are invasive and not routine prior to CRT. Nevertheless, McCulloch is optimistic: "I



McCulloch's detailed models of hearts with dyssynchronous heart failure revealed a close correlation between heterogeneous regional work (below left), which was highly variable among patients, and successful cardiac resynchronization therapy (CRT). In addition, there was a nearly linear correlation between the portion of the left ventricle performing negative work and CRT success (below right). Courtesy of Andrew McCulloch.

actually think we will be able to get the same result with less invasive measurements and use invasive measurements to validate the model," he says. And at that point perhaps this approach will be ready for development into a viable clinical application.

Modeling Who to Graft

If a patient's coronary artery becomes severely blocked with plaque, flow can be improved by bypassing the clogged area with a grafted artery or vein obtained from somewhere else in the patient's body. But vein grafts used for this procedure (coronary artery bypass grafting or CABG) fail at alarmingly high rates, says Marsden, and more often than artery grafts.

When Marsden first began approaching this problem, she planned to model how to optimize graft geometries and placements for specific patients. But clinicians told her that wasn't the challenge; They just wanted to know why certain patients' grafts fail so often. Marsden listened and her team switched gears. In collaboration with Jay Humphrey at Yale University, her group began simulating how veins remodel under changing flow and pressure conditions and then paired those simulations with patient-specific models of post-CABG patients.

Vein grafts are known to experience a big shock when implanted in the arterial system: They are suddenly exposed to a 20-fold increase in pressure. Marsden's team's simulations showed that veins appear to adapt more favorably when the load is applied more gradually. The work is still relatively new, but if it leads to further insights that can be validated in the lab, Marsden says, "ultimately they could result in a clinical solution."

WHAT IS THE BEST TREATMENT FOR THIS PATIENT?

Perhaps the most challenging type of translational modeling and simulation involves looking for better ways to treat patients. In some cases, the status quo is a pretty unpleasant option—so improvements are desperately needed.

Modeling Where to Burn

In addition to modeling the risk of ventricular tachycardia (VT), Trayanova has

Advice, Continued

as automated mesh generation or the use of beam elements in their finite element models. When trying to reduce computational cost, Capelli says, researchers need to determine when good is good enough. "But good enough depends on the question we're addressing," he says. If it's a question of whether a device fits or not, then the models can compromise on numerical accuracy in favor of reducing computational times. But if the model is exploring the risk of structural failure of a device, it requires more precise information, he says.

Commodify it.

In any effort to translate research to the clinic, there is a "valley of death" to be overcome, says **Ahmet Erdemir**, **PhD**, assistant staff in the Department of Biomedical Engineering at the Lerner Research Institute of the Cleveland Clinic. Business savvy and venture funds may be required to take a research-worthy model and make it clinic-worthy, he says.

Heartflow (Taylor), Cardiosolv (Trayanova) and InsilicoMed (McCulloch) are all examples of computer modelers bringing a business mindset to their computational models. Erdemir also has a business-like establishment at the Cleveland Clinic paired to his academic work—Computational Biomodeling (CoBi) Core. His academic research program generates some tools that this fee-for-service facility can use, and CoBi Core generates new ideas that he can feed back into the research program. "My NIH program officer referred to it as my own P41," he says.

Merge with the existing workflow.

For computer models to move into the clinic, they must be useful without greatly disrupting clinical practice. Heartflow's FFR_{CT} is a case in point: It doesn't require any extra protocol in the clinic—not even an extra exam, Taylor says. When the patient's CT is completed, a virtual machine at the clinical site securely pushes anonymized images through a firewall to Heartflow. The results are then automatically sent back to the physician. It's extremely non-disruptive and can be easily integrated into clinical practice.

Parodi has a different approach: he is building his models of plaque composition and progression into a clinical decision support system called ARTreat that can be deployed at the clinic. The entire system is not yet ready for prime time, although some pieces of it—including software for automatic analysis of plaque components from noninvasive imaging—have been tested by cardiologists with positive results.

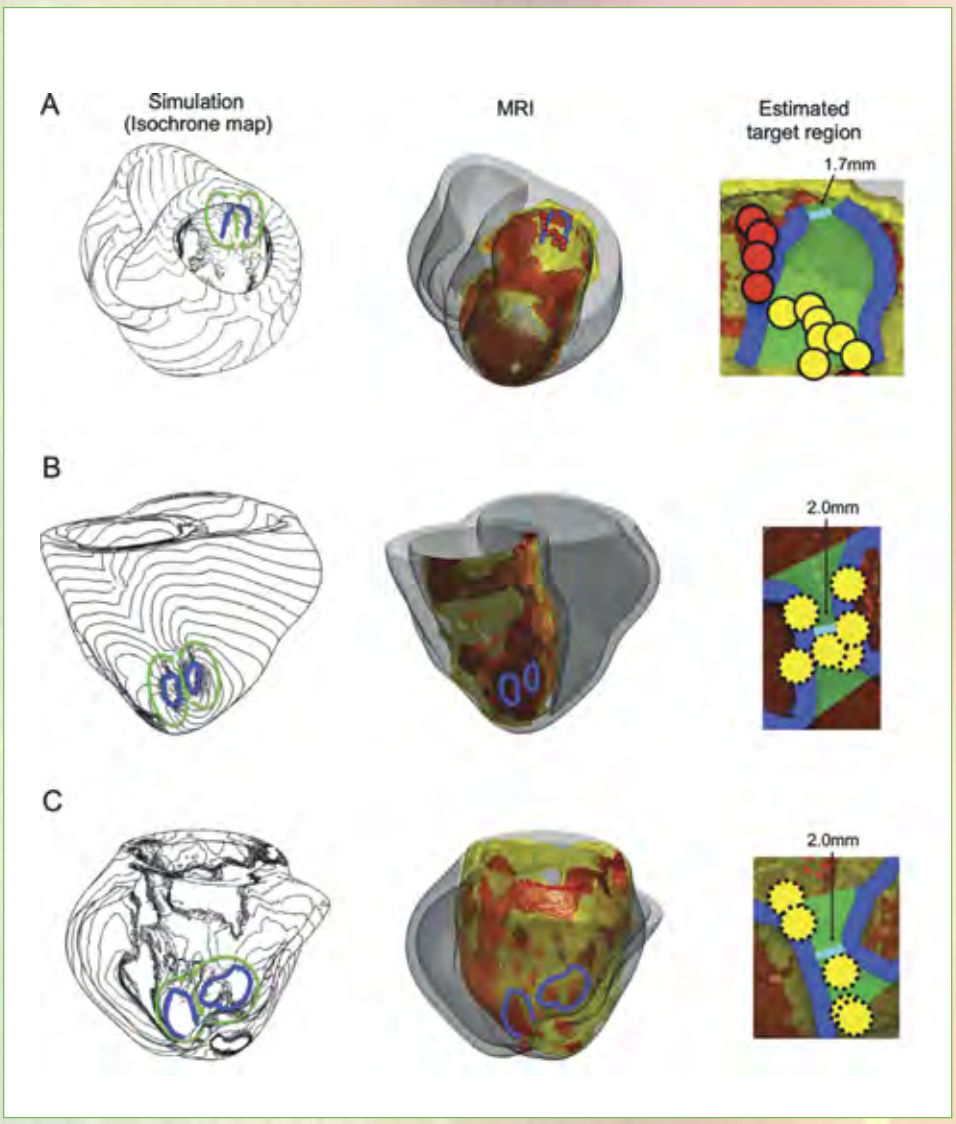
Some models might reach the clinic almost invisibly. For example, if Marsden's Y-graft procedure proves beneficial, it could become widely adopted as a surgical method without further reliance on the model. Similarly, McCulloch's models that determine who will respond to CRT might lead to clinical criteria for deciding who to treat, he says, "possibly obviating the need for patient specific modeling."

Such a result might not lead to money or fame, but it will make a difference in the clinic. And that's what it's all about. □

been modeling the best way to perform a common treatment called ablation—inserting a probe to selectively burn heart tissue as a means of disrupting the circuit that causes VT. It's a brutal six to eight hour procedure: The interventional cardiologist inserts a probe in the heart to cause VT; makes an educated guess as to where to burn to prevent VT; does the ablation; and then shocks the heart back into rhythm. It is then necessary to repeat that aggressive procedure several times until VT can no longer be provoked. Along the way, the electrophysiologist also makes many burns.

In hopes of shortening the procedure, Trayanova and her team have been studying the feasibility of using modeling to predict where a surgeon should ablate. In a paper published in *Heart Rhythm* in 2013, they reported on work in which they performed 30 to 50 simulations of electrical conduction on 13 patient-specific models of VT. It required a lot of computer time, but it was time well spent, Trayanova says. The models blindly predicted ablation sites that the electrophysiologists did in fact use. The team is now working on a follow-up paper reporting on simulations with models of more patients' hearts and demonstrating that if electrophysiologists relied on the simulations rather than guesswork, ablation procedures would be shorter and require fewer burns, Trayanova says.

CardioSolv LLC, the company founded by Trayanova, has been trying to build a more lightweight version of the model, as well as find a way to streamline the delivery of model predictions to the electrophysiologist. "We're scaling back to figure out what are the most important components," Trayanova says.



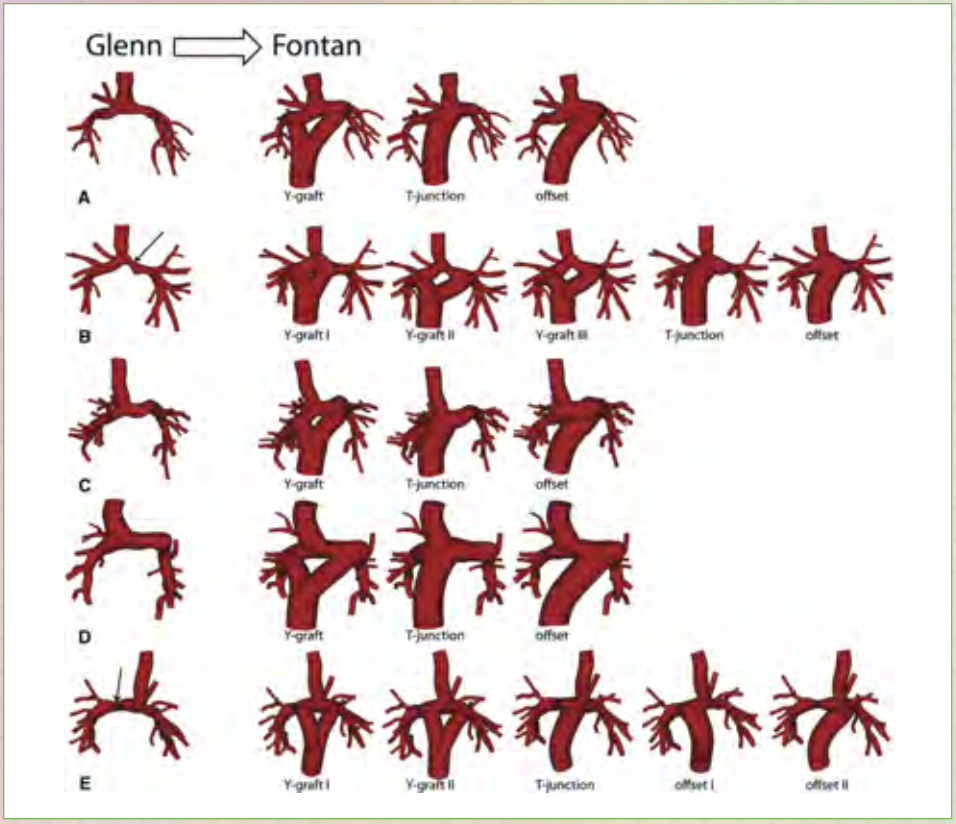
When Trayanova's team simulated ventricular tachycardia (first column) in patients A, B, and C, they identified areas where conduction was blocked (blue lines). In the magnetic resonance imaging (MRI) column, the blue lines from the image-based simulation are co-registered with the actual ablation sites (red circles) on the heart geometry. The last column shows a zoomed-in image of the zone (green) that the simulations predicted as a likely target for successful ablation, along with a cyan line marking the shortest possible line of ablation across the target region. The ablation sites that fell within the estimated ablation target (green area) are indicated by yellow circles and are consistent with the simulations' predictions that ablations in this target zone should be sufficient to prevent VT. Reprinted from Hiroshi Ashikaga,* et al.*, Feasibility of image-based simulation to estimate ablation target in human ventricular arrhythmia,* **Heart Rhythm** *10/8:1109-1116 (2013), with permission from Elsevier.

Modeling Surgical Corrections

Some children are born with only one ventricle in the heart—a dangerous condition that is fatal if left untreated. Typically, cardiologists correct the problem by performing three open-heart surgeries, culminating in what's known as the Fontan surgery: They insert a Gore-Tex graft in various conformations (typically a T-junction or an offset T) to redirect and improve blood flow.

Because surgeons wondered if the existing grafts were optimal, Marsden and her colleagues decided to model and simulate the procedure using several alternative graft shapes. The simulations led to a proposed Y-graft modification of the procedure that appeared to improve blood flow and energy efficiency. A pilot study in six patients found that the surgery is technically feasible and has outcomes that are at least similar to the standard of care, Marsden says.

While the Fontan procedure saves lives, many patients can still develop long-term complications such as pulmonary arteriovenous malformations, Marsden says. Long-term follow up data on the Y-graft is therefore needed, Marsden says. "We may



Marsden and her colleagues modeled a novel Y-graft version of the Fontan procedure, which corrects for a congenital heart defect in which babies are born with only one ventricle. This diagram displays multiple different surgical design options in five different patient anatomies (A to E). Computational fluid dynamics simulations predicted the Y-graft would lead to improved blood flow and reduce energy losses. Reprinted with permission from Weiguang Yang,* et al.*, Hepatic blood flow distribution and performance in conventional and novel Y-graft Fontan geometries: A case series computational fluid dynamics study,* J Thorac & Cardiovasc Surg *143/5:1086-1097 (2012).

not find out if it improves outcomes for another 5 to 10 years."

Modeling the Device/Patient Matchup

While tight working relationships between modelers and clinicians are essential to any kind of biomedical modeling for the clinic, they may be even more important when modelers work at the interface between medical device engineers and clinicians.

Melissa Young, PhD, project scientist in the biomedical engineering department of the Cleveland Clinic and assistant professor at the Cleveland Clinic Lerner College of Medicine, Case Western Reserve University, has been working closely with a multidisciplinary team that is developing a mitral valve frame—a kind of valve stent—that can be delivered noninvasively. The team brings together modelers, surgeons, imaging experts, device designers, and testing engineers, not to mention the Cleveland Clinic's innovations group, an entity that seeks industry sponsors and other funding for projects such as hers.

Because the mitral valve frame will be delivered by a catheter, it has to start small and then expand into place. It therefore needs to be both strong and flexible while also having a good fit with the mitral valve anatomy. Using simulations of various stent designs and mitral heart valve boundary and loading conditions, Young's team identified a few favorite designs out of several dozen possibilities. "Manufacturing stents for evaluation is expensive," Young says. "If you can take 25 designs and narrow them down to three that would be best for fatigue, gross expansion, and the ability to anchor successfully, that's really helpful."

Young is also developing a computer tool to guide surgeons in selecting stents for their patients with peripheral artery disease, a condition that affects about eight million Americans and carries health care expenditures of $3.7 billion annually. Currently, surgeons have a choice of just a few stents to help these patients; and they might tend to select the ones they are used to—or what the hospital carries. "But that's not necessarily the best fit for a patient," Young says.

When completed, Young's tool will allow surgeons to try different devices on a virtual map of the patient's arteries. This map, which is a mesh inferred from patient-specific intravascular ultrasound data, shows not only arterial structure but also plaque composition, a characteristic that affects arterial mechanics and, in turn, drives stent choice or placement.

Claudio Capelli, PhD, research associate in the Centre for Cardiovascular Imaging at University College London Institute of Cardiovascular Science, also works on matching devices to patients. He has been developing patient-specific models to explore percutaneous pulmonary valve implantation (a procedure for replacing the pulmonary heart valve using a catheter). The procedure is extremely beneficial but still not widespread, Capelli says.

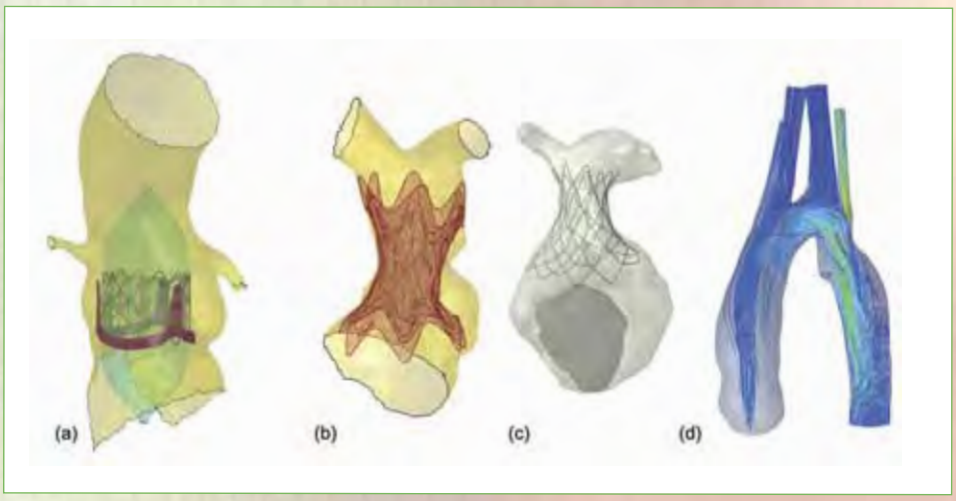
Capelli works in a team that was established by **Silvia Schievano, PhD**, a decade ago and is located within a pediatric hospital where the engineers participate in clinical meetings for non-routine, difficult cases. "We offer the possibility of simulating an intervention before it happens, especially when there is doubt about which device to use or which size to use because of interaction with the anatomy," he says.

Starting from images, his team constructs anatomical models of a patient's heart, which might take two or three hours, he says. Next, they simulate the implantation of a handful of devices that might be appropriate based on the cardiologist's in-

"Manufacturing stents for evaluation is expensive," Young says. "If you can take 25 designs and narrow them down to three that would be best for fatigue, gross expansion, and the ability to anchor successfully, that's really helpful."

dications. The simulations then determine the stresses on the device and heart. Finally, the team offers its insights to the cardiologist who makes his or her own decision about what to do. "Whether they agree with our prediction or not," he says, "it still provides us a huge source of data to follow up and validate our predictions."

Thus far, Capelli's team has provided this kind of predictive advice in about ten patient cases. In one case, his team was asked to determine the optimum stent size to correct a narrowed aorta with very unusual anatomy. "We needed to cover an aneurysm without covering access to a small vessel on the other side," he says. His team did a 3-D reconstruction of the anatomy and used finite element analysis and computational fluid dynamics to recommend a particular device. The cardiologist followed the team's suggestion and the procedure was successful, Capelli says.



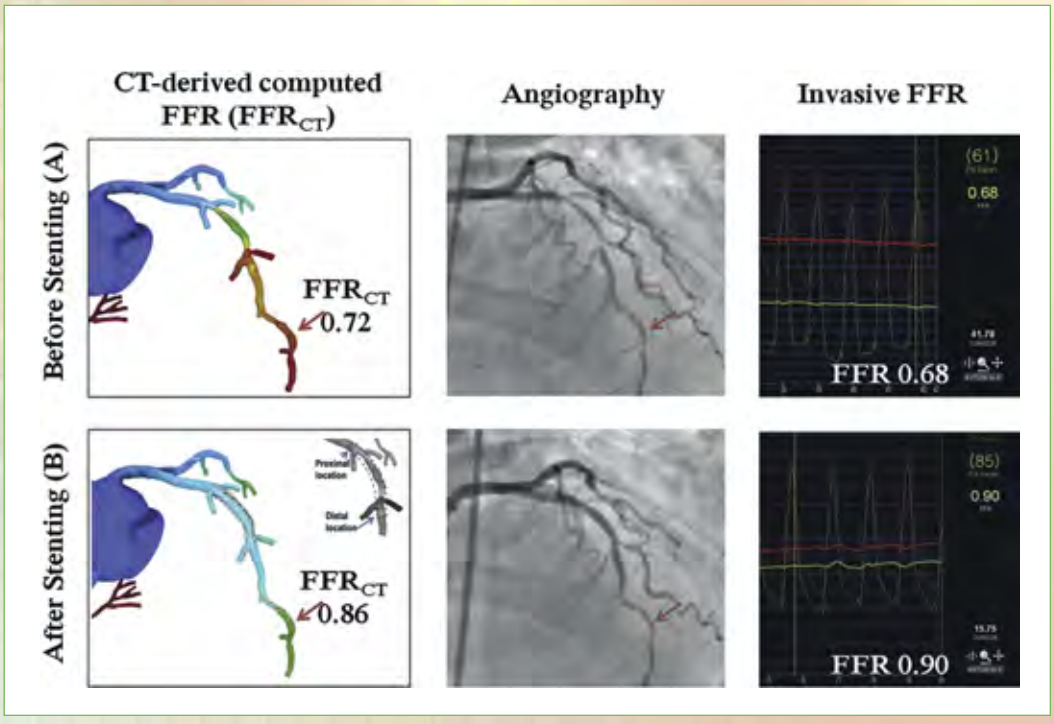
Capelli's group has performed patient-specific simulations for a variety of interventional procedures including (a) transcatheter aortic valve implantation: case of valve-in-valve procedure; (b) percutaneous pulmonary valve implantation: stent-graft; (c) percutaneous pulmonary valve implantation: bare metal stent; (d) flow distribution following the implantation of a stent-graft within aortic coarctation. (Simulations by C Capelli and GM Bosi).

Sometimes modeling also gets it wrong. In one case, Capelli's group selected a device with a certain size (the largest available). But when the cardiologist did a balloon sizing (to evaluate the location), he found a less resistant wall than what the model predicted. "The wall didn't guarantee a good anchoring," Capelli explains. Since the recommended device was already the biggest available, no device was implanted. "So the cardiologist always has the last word," he says.

Capelli and his colleagues continue to refine their models for device choice, and have also developed a virtual library of 41 different devices and 600 to 700 models, most of them related to congenital heart disease. Capelli hopes device-development companies will use these libraries to test various devices on particular target populations. "Having the possibility to play virtually with these anatomies can help reduce animal tests and replicate more realistic conditions in the testing of devices," he says.

Virtual Stenting

HeartFlow is also entering the realm of simulating alternative treatments. To demonstrate his latest project, Virtual Stenting, Taylor pulls out his iPad and loads a 3-D image of a patient's heart and arteries. He then touches the narrowed sections of the artery to get a pop-up showing the FFR_{CT}. If the FFR_{CT} is less than 0.8, he selects a virtual stent from a menu, drags it into place, re-sizes it, and then touches the artery to see how the stent changes the FFR_{CT}. The software was successfully tested prospectively on 44 patients: FFR_{CT} for the patients closely matched the invasively measured FFR both before and after stenting. The work was published in *JACC: Cardiovascular Interventions* last year, and is perhaps the clearest example yet of how lightweight cardiovascular computer models could find their way into the practice of medicine. □



Heartflow is developing a virtual stenting application to evaluate whether a stent will change a patient's stenosis. Here, before stenting (top images), stenosis of the left anterior descending (LAD) coronary artery is demonstrated by a noninvasive FFR_{CT} of 0.72 and confirmed by invasive coronary angiography and invasive FFR (0.68). After virtual stenting (bottom images), noninvasive FFR_{CT} demonstrated no ischemia in the LAD, with a computed value of 0.86. Invasive FFR after stent implantation was 0.90. Reprinted from Kyung-Hee Kim, et al., A Novel Noninvasive Technology for Treatment Planning Using Virtual Coronary Stenting and Computed Tomography-Derived Computed Fractional Flow Reserve, J Am Coll Cardiol Intv. 7(1): 72-78 (2014).