AI Will Increase MRI's Accessibility, Accuracy, and Affordability for Cardiac Diagnostic Imaging

CLD talks with Bob S. Hu, MD, Director, Cardiovascular Imaging at Sutter Health — Palo Alto, California, Chief Medical Officer, HeartVista, and Itamar Kandel, CEO, HeartVista.

HeartVista's October 2019 FDA clearance for its One Click Cardiac MRI package was announced against the backdrop of the June 2019 publication of the MR-INFORM trial in the New England Journal of Medicine.[1] MR-INFORM found that among patients with stable angina and risk factors for coronary artery disease, myocardial-perfusion cardiovascular MRI was associated with a 20% lower incidence of coronary revascularization than fractional flow reserve (FFR) and was noninferior to FFR with respect to major adverse cardiac events.[1]

How might the results of the MR-INFORM trial[1] change how MRI is perceived and utilized?

Bob S. Hu, MD, Director, Cardiovascular Imaging at Sutter Health — Palo Alto, California, Chief Medical Officer, HeartVista: Every noninvasive test has traditionally been used to try to guesstimate what will be found in the cath lab. The cath lab has been the gold standard of accuracy for determining what we will ultimately do in order to treat a patient. But, as you know, the 2009 publication of the FAME trial[2] showed us that anatomy was not even the cath lab gold standard anymore, but that a physiologic test such as fractional flow reserve (FFR) is in fact more accurate in predicting outcome. Since then, the noninvasive tests have shifted focus, trying to look for ways of estimating the cath lab-derived FFR, in nuclear but particularly in computed tomography (CT) imaging. The MR-INFORM trial is different; it is the first noninvasive test evaluation that presupposed that the angiographic anatomical image is no longer considered the gold standard — FFR is. The question is, could the invasive FFR itself be improved upon? That is what MR-INFORM sought to answer. The trial was conducted in mostly European centers and used clinical outcomes as the final arbiter as to whether an imaging technique was accurate. MR-INFORM was designed as a noninferiority test; the MRI should be as good as the basic invasive FFR in order for the trial to be considered a success and indeed, MRI was determined to be so, in terms of predicting outcomes. At the same time, diagnostic imaging with MRI was able to reduce the number of patients going to the cath lab by 20%, saving them from a procedure that they did not necessarily need. That is important, since approximately 30% of catheterizations do not result in a procedure because there is no need for an intervention. The MR-INFORM trial does

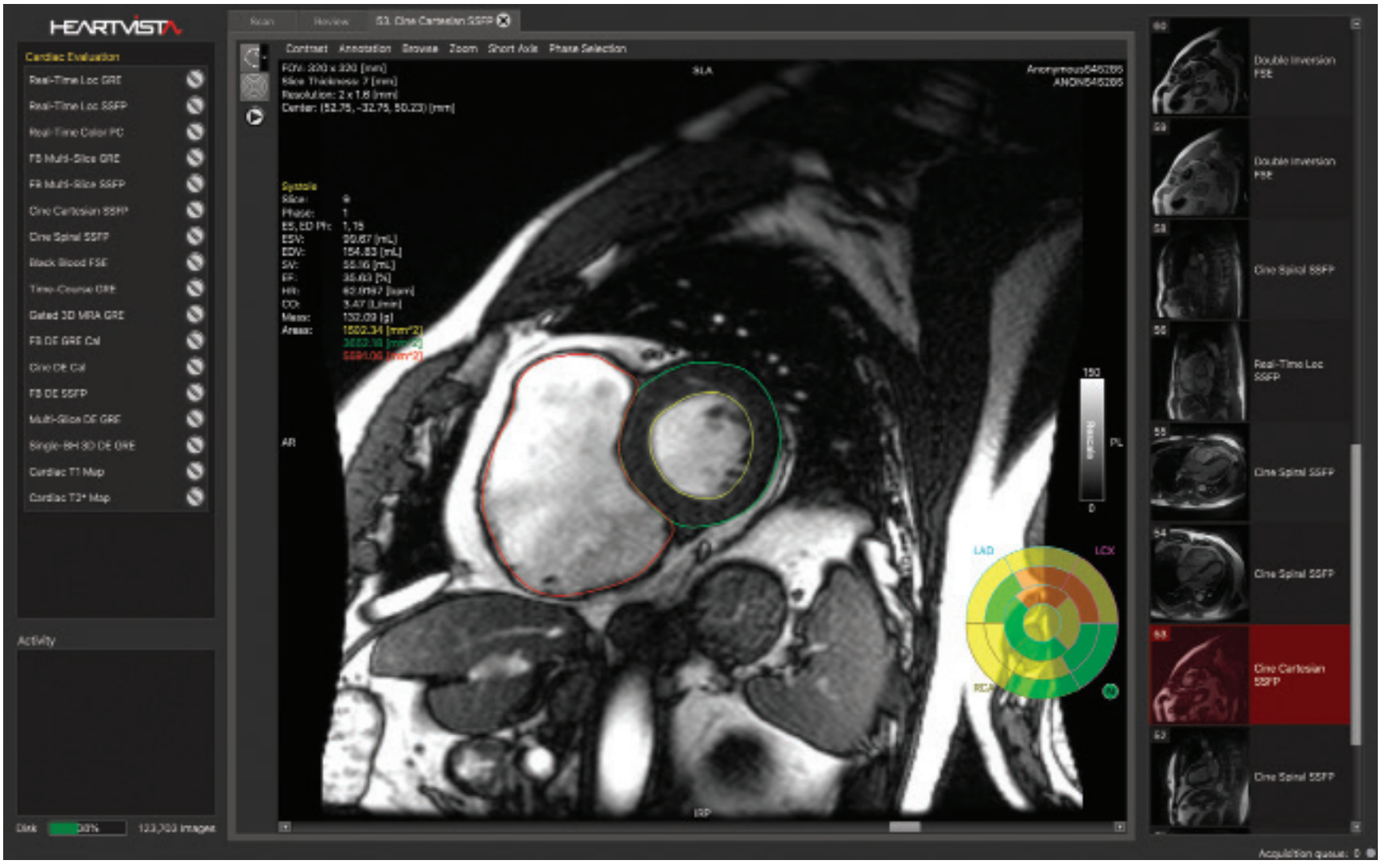

Figure 1. User interface for HeartVista's FDA-cleared cardiac MRI acquisition product showing complete analysis of left-ventricular function including contouring and a bullseye-style plot of regional wall motion. Functional measures such as ejection fraction can be obtained with the patient on the table and without operator intervention.

have some drawbacks, with the most important being that it budgeted only about an hour to do the MRI study. In clinical practice, it is possible to see numbers perhaps as low as 45 minutes to do a stress MRI study, but normally, we see numbers upwards of an hour and a half, depending on how the study was conducted, the personnel involved, etc. This is in stark contrast to the current HeartVista protocol, which is designed for an MRI study to be performed comfortably in less than 20 minutes. These important results of the MR-INFORM trial can be paired with the use of HeartVista's One Click Cardiac MRI platform to make MRI image acquisition more realistic in terms of everyday practice.

What have been the challenges with MRI that have precluded it from more widespread use?

Dr. Hu: There are several factors, although in cardiology practice in Europe, MRI has actually been adopted much more widely than it has in the United States, and it is accelerating. Part of the issue is that, frankly, Europeans pay more attention to quickly deriving the benefits of MRI into the clinical arena because they have a national health care system. Savings in terms of money and accuracy is very important to them. For instance, the 2012 CE MARC study[3], led by John Greenwood, demonstrated that cardiovascular magnetic resonance (CMR) imaging is probably the most cost-effective way[4] to do an ischemia evaluation for coronary artery disease. On the strength of that study, there has been significant conversion towards that test. (Note that Dr. Greenwood is also the second author on the MR-INFORM trial.) I think cardiologists as a whole are very data driven. MRI is no longer just one of several noninvasive tests. MRI is now, compared to the gold standard, just as good. It also saves on unnecessary caths and that is a different kind of gain as well. MRI has no radiation compared to nuclear imaging and provides more data compared to any other modality. It offers scar mapping to look at viability and of course, is the gold standard on left ventricular function. Not to mention the fact that in addition to ischemia evaluation, it is also the most accurate in terms of quantitating valvular regurgitation and has been shown to actually be better than quantitative echocardiography at predicting outcomes for mitral valve surgery for regurgitation.[5] There are ongoing discussions in the American Heart Association guidelines committee in terms of recommendations regarding MRI use. There is definitely reason to think that MRI could potentially become one of the first indications for ischemia evaluation.

Can you tell us about the platform and software that HeartVista created and how it solves some of the issues that exist with MRI?

Dr. Hu: Matthias Stuber is a professor at University of Lausanne, Switzerland in Switzerland. He evaluated the movements made by an MRI technologist while performing a cardiac MRI exam. He clocked the technologist doing a few hundred mouse clicks to conduct an MRI exam for one patient. MRI is like a giant scientific experiment, or in more plain terms, like cooking. Several ingredients are required for the recipe to come out just right, i.e., to give you the data that you want. MRI's flexibility can give us all sorts of different images: blood flow, heart muscle, scarring, and ischemia. But in order to get this one machine to do everything you want, it requires tinkering in order to get everything just right. That is what an MRI technologist must do in order to create a good result that is interpretable and actionable for the patient. It takes a long time to train someone well, and it is not uncommon for there to be a resulting specialization: a head tech, a heart tech, and so forth. What HeartVista did was to take all the decision making and resulting decisions, or "mouse clicks," and drop that number down to just a couple clicks instead. Our HeartVista Cardiac Package takes control of the existing MRI machine, and performs an automated cardiac ischemia exam from start to finish with only "one click" of the mouse. Our model is called "One Click," and sometimes it may be a couple clicks, but the idea is that all of those imaging adjustments are automated by HeartVista's AI software. During MRI image acquisition, any adjustments are normally made by the MRI technologist, who may determine that the image size needs to be a little bigger or the contrast of a particular artery should be adjusted, in the case of the heart. They might decide there is a need to better enhance a scar, or reduce blurring because of the motion, as well as shimming the magnetic field so that it is flatter and less likely to cause image artifacts. All these minute adjustments involve the technologist evaluating the image and identifying problems. After they identify a problem and what is necessary for the desired result, they make some tweaks, get another picture, look at it again, and so on and so forth. It is a gradual tuning process. HeartVista's AI platform, embodied with the data of millions of images from thousands of patients, is able to look at the same image instantaneously and the software platform has a response time of less than a couple hundred milliseconds. It takes a look, makes a decision immediately, makes a change, and then repeats that process very, very quickly. That is the difference between what HeartVista is doing and what an individual person might do. Don't get me wrong — a good MRI technologist has years of experience and I would not say that at this moment in time, HeartVista's platform is going to top out against someone with 20 years of experience in MR imaging. The idea is that this person can become a supervisor, watch the machine, and then look at the results and determine if it made the right decisions. All the mundane stuff of getting to the final results can be done much, much faster, and that is the difference between what HeartVista does and what is conventionally done.

Itamar, as HeartVista's CEO, how do you see the company positioned?

Itamar Kandel, CEO: I joined HeartVista in June 2019 to commercialize the company's innovative science and technology, and bring this technology to the wider public. The company started in 2012, and was funded with a series of grants from the National Institutes of Health (NIH) and investments from Khosla Ventures, among others. We have achieved a lot since our launch: the actual science behind the product is complete, the technology has been built, and we have obtained patent protections and FDA clearances, with the biggest FDA clearance in October 2019 for the One Click MRI platform. In addition, the use of the One Click MRI package does not require creation of new CPT codes or negotiation with payers. Doctors can bill CMS and payers using the same CPT codes that they already use for cardiovascular magnetic resonance (CMR). We now have a wonderful set of components to start expanding our business.

Dr. Hu: Our initial group of patients that have undergone scanning, approximately 2000, were based on a prior FDA plan that was not AI driven. The AI-driven aspect received FDA clearance in October 2019. Being able to utilize the AI portion means that we use the same MRI sequence software that I have now used clinically for 3 years in over 2000 patients and endow it with "smartness", if you will, so that the software can now do that same type of scan on its own.

Itamar: What we are doing is different from the majority of "AI in Radiology" companies, who tend to focus on the post-processing phase. This means that after the machine is finished creating images, the post-processing companies implement an AI algorithm that tries to identify something clinically interesting about the images. HeartVista, on the other hand, actually runs the machine all the way from generating the pulse sequences, to reconstructing the images, to manipulating the magnetic field that yields the desired diagnostic-level images. That control of the MRI machine allows us to do things that no other "AI in Radiology" company can do, because the patient is still in the machine while the analysis is done. For example, if our platform identifies an anomaly, it can automatically acquire more images so the cardiologist gathers all relevant information in one go, when he or she looks at the images. AI inclusion means we further reduce the amount of time that an exam takes and reduce the level of expertise needed from the technologist running that machine to a single or a couple of clicks of a button.

Can you describe how the AI aspect functions?

Dr. Hu: Let's say I'm going to make an image with a cut through the body in a certain orientation. The kind of data we typically use, as humans, involves recognizing things in the image that are helpful

to orient ourselves and allow us to make further decisions. An MRI technologist may recognize something in the particular view of the anatomy that is helpful. That recognition allows them to orient themselves in order to take the next image on the basis of the previous image. Let's say we want to bisect a face. First, we have to figure out where the nose is and then where the two eyes are located. Then we can put something on the head to split the head in half by looking at the left and right eyes, and putting the cut an equal distance away, splitting it at the nose. That information could be gleaned from a normal exam and you can teach a machine to do exactly the same thing. There is a lot more to it, of course. There are a multitude of things to take into account and each have to be individually considered. We have several neural nets running inside the system, all attuned to different aspects in order to approximate human behavior in obtaining the final imaging result.

Have you been working with any imaging partners?

Dr. Hu: Yes, our system is now cleared for use with GE Healthcare's MRI platform and we also have a development agreement with Siemens Healthineers.

How do you see AI moving further into the cardiology space?

Dr. Hu: Most of our AI work has been focused on the acquisition side. Focusing on the acquisition side of data means that we must consider the following series of questions. First of all, did we collect the necessary data? Second, does that data have the appropriate image quality? Finally, we think that the next step is enhancing the actual diagnosis. Probably for the next year, our primary focus is going to be on acquisition. We do already have some post-processing analysis. As the images come out of the machine, our current product will immediately analyze the images for things like ejection fraction, left ventricular mass, cardiac output, and so forth. That is just done as a matter of course. Our plan is to use the available data to detect, for instance, somebody's ejection fraction is very low, and figure out whether our protocols should then adjust to acquire more data, to further understand why the ejection fraction is low. Similarly, if an infarct is found, that changes what happens next. New sequences would need to be initiated rather than what was originally intended. It requires a level of expertise that is deeper than just being able to tell whether something is good or bad, or whether you have the right slice position. Eventually, 10 years down the line, we are hoping our product will be as good as any top physician and technologist combined.

Itamar: AI is not going to put doctors out of business. For at least the next 20 years, there will always be a need for the human as part of the equation. AI will start being a component of medicine and it is going to be partnering with humans. It will involve humans giving up what computers can do better and zeroing in on what humans can do better. It is the physicians that are not equipped with AI technology who are going to become obsolete and go by the sidelines.

Dr. Hu: For long-term planning, we can make MRI more available to more people. Once MRI can be done quickly, we can bring the price down to something more affordable and address some of the cost issues in healthcare. ■

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HeartVista Receives FDA 510(k) Clearance for One Click Cardiac MRI Package

In October 2019, HeartVista received 510(k) clearance from the U.S. Food and Drug Administration to deliver its artificial intelligence (AI)-assisted One Click MRI acquisition software for cardiac exams. Despite the many advantages of cardiac MRI, or cardiac magnetic resonance (CMR), its use has been largely limited due to a lack of trained technologists, high costs, longer scan time, and complexity of use. With HeartVista's solution, cardiac MRI is now simple, time-efficient, affordable, and highly consistent.

"HeartVista's Cardiac Package is a vital tool to enhance the consistency and productivity of cardiac magnetic resonance studies, across all levels of CMR expertise," said Dr. Raymond Kwong, MPH, Director of Cardiac Magnetic Resonance Imaging at Brigham and Women's Hospital and Associate Professor of Medicine at Harvard Medical School.

A recent multi-center, outcome-based study (MR-INFORM), published in the New England Journal of Medicine, demonstrated that non-invasive myocardial perfusion cardiovascular MRI was as good as the gold standard method of invasive fractional flow reserve (FFR), to guide treatment for patients with stable chest pain, while leading to 20% fewer catheterizations.

"The recent NEJM study further reinforces the clinical literature that cardiac MRI is the gold standard for cardiac diagnosis, even when compared against invasive alternatives," said Itamar Kandel, CEO of HeartVista. "One Click makes cardiac MRI exams practical for widespread adoption. Patients across the country now have access to the only AI-guided cardiac MRI exam, which will deliver continuous imaging via an automated process, minimize errors, and simplify scan operation. Our AI solution generates definitive, accurate and actionable real-time data for cardiologists. We believe it will elevate the standard of care for cardiac imaging, enhance patient experience and access, and improve patient outcomes."

HeartVista's FDA-cleared Cardiac Package uses AI-assisted software to prescribe the standard cardiac views with just one click and in as few as 10 seconds, while the patient breathes freely. A unique artifact detection neural network is incorporated in HeartVista's protocol to identify when the image quality is below the acceptable threshold, prompting the operator to reacquire the questioned images if desired. Inversion time is optimized with further AI assistance prior to the myocardial delayed-enhancement acquisition. A 4D flow measurement application uses a non-Cartesian, volumetric parallel imaging acquisition to generate high-quality images in a fraction of the time. The Cardiac Package also provides preliminary measures of left ventricular function, including ejection fraction, left ventricular volumes, and mass.

HeartVista will present its new One Click Cardiac Package features at the American College of Cardiology (ACC.20) Scientific Sessions (Booth #9079).

About HeartVista. HeartVista's technology originated at the Stanford Magnetic Resonance Systems Research Laboratory. HeartVista is funded by Khosla Ventures, and the National Institute of Health's Small Business Innovation Research program. For more information, visit www.heartvista.ai ■

Bob S. Hu, MD, Director, Cardiovascular Imaging at Sutter Health — Palo Alto, California, Chief Medical Officer, HeartVista

Itamar Kandel, CEO, HeartVista

Contact Itamar Kandel at itamar@heartvista.com