By James Borwick

Reinventing the ECG

Did you ever hear the story about how Hedy Lamarr came up with the basic idea behind cellular and wireless technologies? Between films, she worked with a music composer to create something called frequency hopping (also known as spread spectrum) in order to improve torpedo guidance in World War II. Years later, the patent was rediscovered and applied to modern communications technology, paving the way for cell phones, pagers, and Wi-Fi.

Dr. Joseph Shen may not be poised to challenge Ms. Lamarr's celebrity status, but he hopes he has done something at least as important by taking the ordinary ECG and turning it into a noninvasive means of detecting coronary obstruction with nearly the same accuracy as an angiogram. "For the first time in their careers," says Dr. Shen, developer of the 3DMP system and managing principal of Premier Heart, which sells it, "primary care physicians will be able to [perform primary diagnosis of coronary artery disease] in their own office. They are going to perform like good cardiologists."

ACCURATE AT 40% AND UP

"This is a noninvasive technique that, out of a population where the pretest probability of coronary disease is low, accurately identifies patients with a high likelihood of having a coronary obstruction 40% severe or more," says Dr. John Strobeck, director of the heart failure program at the Valley Hospital in Ridgewood, New Jersey, and director of the Heart-Lung Center in Hawthorne, New Jersey. "This is 97% as accurate as an angiogram at identifying people who have blockage 40% or greater."

The 3DMP system represents "a breakthrough technology," he says, "because it is extracting information from an old tool, the ECG, that has been used to death as people have tried to milk every last bit of information from it. Many times the ECG is misleading or erroneous in its ability to detect problems because the analysis, up until now, has been in the time domain. This technology ignores the time domain and analyzes the ECG in what is called the 'frequency domain,' which has so many more moving parts."

Dr. Shen puts it this way: "Conventional ECG, as all physicians know, is based on the theory that all the information from the heart muscle can be reduced into a single dipole, plus or minus. Millivolts versus milliseconds, that's how the ECG graph is plotted. That information is then analyzed one lead at a time and one cycle at a time. Typical analysis of the ECG involves focusing on different segments, such as the ST segment, or T waves, et cetera. And this is good for detecting arrhythmia, but it's very poor for detecting ischemia. The sensitivity for people with severe coronary ischemia is only 20%. If you have a myocardial infarction, it rises to 50%, but it has to be [conducted] at the time the MI is taking place."

Dr. Shen notes that because of the way information is extracted using conventional ECG, condensing it into a single dipole, abnormal readings may normalize over time, creating a simplified image of the heart. He likens it to drawing a human being as if it were a stick figure.

"What our system does," Dr. Shen says, "is use two left ventricular leads (V_5 and II)—because our testing over the years has shown that these leads give the most information—to extract information recorded simultaneously from multiple cycles. Then we convert this information into the frequency domain, that is, hertz instead of milliseconds and power output instead of voltage." *continued*

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—Dr. Joseph Shen, managing principal, Premier Heart, Port Washington, New York

'INFORMATION THAT'S NEVER BEEN LOOKED AT BEFORE'

"Dr. Shen likes to call the conventional ECG a reductionist method," says Dr. Strobeck, "because it tries to reduce everything to a simple common denominator, and the way to do that is to analyze it in the time domain. The real story is what's going on with all the component frequencies that are being generated by all the different living cells in different regions and they're not all the same, they're not all going to be in synchrony together. There's just a lot of information there that's never been looked at before.

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"Any living organ emits energy at a whole host of varying frequencies and a normal organ has a frequency profile that is completely different from an organ with a pathological problem. The fascinating concept here is that Dr. Shen decided that embedded in the typical information is probably all the information he needs to make an accurate diagnosis of some of the pathological conditions that are present. Initially, nobody could figure out how to do it, but he applied some engineering and some mathematical principles relating to the interaction between solids and liquids that opened the door for him to make these kinds of observations.

"Almost any biological signal could be analyzed this way. There's undoubtedly a huge amount of information embedded in the EEG, for example, that would give us so much more insight into the health of the brain besides just detecting whether a person has had a seizure or not. It's a fascinating new way of thinking about biological signals and biological electric potentials. This could be adapted for use in cancer detection, for example. It has a lot of potential uses."

According to Dr. Shen, the mathematical model applied in 3DMP treats the heart muscle as a "semi-elastic solid," highlighting the relationship between the activity of the muscle and the flow of blood, and providing a foundation from which to project the ECG signals and translate them into six functions that reflect and quantify that relationship. Dr. Shen compares the standard ECG to a single point of light versus the 3DMP model, which expands the ECG data like light through a prism, allowing for a much deeper output than has previously been possible.

"We have used the same measurements of these six functions in 7000 people, aged 14 to 97 (divided equally between male and female subjects), who are normal. In other words, we have established a database of normal controls across the six functions in order to determine the normal range of response." In addition, says Dr. Shen, "there is a second database of 28,000 patients who have been identified as abnormal" in order to provide points of comparison across a range of coronary pathologies.

"When you record the electrical activity of the heart from the surface of the body, you're recording a summation of all of the electrical forces that are inside the heart—they all flow together to create one signal," Dr. Strobeck points out. "So all of the data become embedded in that signal, but things that are happening on the anterior and posterior walls of the heart could cancel each other out and might make it appear there is no abnormality. But using the 3DMP ECG, you can measure frequencies specific to the anterior wall of the heart, and frequencies specific to the posterior wall of the heart, and reliably indicate the heart is experiencing problems in the two locations."

CLINICAL UTILITY AND EVIDENCE

"Primary care physicians take care of about 85% of people with coronary disease and ischemia," says Dr. Shen, "and the problem is that they are unable to accurately identify them using the routine ECG and clinical judgment. Unfortunately, many of these patients fall below the radar, due to a lack of symptoms, although they have advanced late-stage disease, and will often test normally using conventional ECG and stress test modalities." Dr. Shen cites the recent death of journalist Tim Russert: "He went in for a stress test and the results were normal, and all of a sudden he has a heart attack because he likely had single-vessel disease."

New sophistication for an old technology. The 3DMP system of ECG interpretation has shown promise as a tool for early detection of ischemic heart disease. It converts information from leads V_5 and II into values based on frequency, rather than simple time, and sends the results to a central database of findings from thousands of patients. The central system replies with an ischemia score, a severity report, and a clinical decision tree. The device shown here is the "laptop" version of the system; there is also a pushcart version.

The 3DMP system uses a probability score of 0 to 22, where a score of less than 4 indicates a very low risk of coronary blockage. Dr. Strobeck illustrates the use of this scoring system with the common scenario of a patient with atypical chest pain and abnormal stress test findings. A score of less than 4 on a 3DMP test would support a good degree of confidence that the stress test result was a false positive and, therefore, would delay performing an invasive coronary angiogram.

"That's how accurate this is," says Dr. Strobeck, adding, "Urgent care physicians take care of a whole lot of people complaining of chest pain that they fear is coming from their heart. This allows physicians to reassure patients with probability scores less than 4, and to refer those with scores above 4 to cardiology specialists for consultation and possibly more testing."

Dr. Shen says that clinical trials of the 3DMP system have involved a total of 1100 patients in six countries and have produced the following aggregate results: sensitivity, 93% to 94%; specificity, 85%; and negative predictive value, 94%.

ADMINISTERING THE TEST

The 3DMP examination, which "any office staff" can be trained to do, according to Dr. Shen, requires connecting the patient to four limb leads and one chest lead. When the patient has achieved his or her resting heart rate, three 82-second ECG samples are taken. The samples are then run through a program on the physician's laptop computer, compressed, and sent over the Internet to Premier Heart's central database, where they are mathematically expanded and compared with known levels of coronary blockage.

"All this happens in seconds," says Dr. Shen. The test tells the physician whether blockage is present or absent, though it does not indicate the exact location of the blockage, which requires angiography and imaging technologies.

Dr. Shen describes the 3DMP as a first-line technology, although he predicts that with further development, 3DMP may be able to give more precise information about ischemia location. "Right now, this version is good enough to tell people how many heart muscle cells are sick due to ischemia, and it will provide you with a score, a severity report, and a decision tree for the physician to act on."

The list price for the system is $29,500, and there is a $50 charge per test for accessing the database to determine the patient's score. Reimbursement for the procedure in the New York City area, for example, ranges from $150 to $250. The technology is new, and at present about 100 units have been sold, primarily in the northeastern United States.

PERSONAL EXPERIENCE

"Our ability to measure ischemia up until now has not been that great," says Dr. Strobeck. "Even with nuclear stress testing we can only detect the most severe forms. [3DMP] is actually giving us insight into the presence of ischemia when the stress test is negative. I've been using it since February of 2008 and the experience has been very good. We've identified several people who had no outward signs or symptoms of blockage, who went on to have angiography, and turned out to have blockage that required stenting. There's a huge population of people with blockage that have absolutely no symptoms or outward signs, and this will help detect and identify those people without them having the risk of going through a coronary event." UC