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iSTORY

HISTORICAL PERSPECTIVE

Stress Myocardial Perfusion Imaging—The Beginning. . .

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"There are no problems—only opportunities to be creative."

Dorye Roettger (1)

Myocardial perfusion imaging was developed to meet the need to noninvasively detect the presence and extent of coronary disease. In 1971, the diagnosis of coronary disease was made by coronary angiography, a procedure that was celebrating its 12th birthday. Selective coronary angiography was developed following the chance observation by Mason Sones that direct intracoronary administration of contrast media could be done safely (2). Echocardiography was yet to be invented. The technology, though advanced for the time, was still hazardous. Cardiologists sought a technique that could be used to help select patients for catheterization. This was particularly important, because Rene Favaloro developed coronary bypass surgery in 1967 (3), and revascularization was available as therapy for patients with severe coronary disease.

In a series of articles published from 1956 to 1960, Leo Sapirstein established the principles required to use a soluble tracer to measure the distribution of cardiac output (4–6). He described 2 key characteristics the tracer must have: rapid clearance from the blood, and high extraction by the organ(s) of interest. One of the tracers that Sapirstein evaluated was K-42, a beta-emitting nuclide with an 18% gamma at 1.5 meV, which made this tracer unsuitable for imaging. The biodistribution studies in animals demonstrated the feasibility of potassium tracers to distribute in proportion to cardiac output in multiple organs, including the myocardium. In the mid 1960s, there was growing interest in developing tracers to image the myocardium to diagnose myocardial infarction. Hurley et al. (7) developed another isotope of potassium, K-43, with better imaging properties. They tested K-43 in humans and found a high sensitivity for the detection of myocardial infarction.

From 1968 to 1970, as a fellow in Nuclear Medicine at Johns Hopkins, I had worked with Barry Zaret and Bert Pitt on the development of gated blood pool imaging to noninvasively measure global and regional left ventricular function (8,9). In 1970, I had to fulfill my military obligation and was assigned to Nuclear Medicine at Travis Air Force Base with Neil Martin, the head of Nuclear Medicine. When Zaret completed his cardiology fellowship at Hopkins in 1971, he also had to fulfill his military obligation and, by chance, was assigned to Travis. When Zaret arrived, we agreed to continue our research in noninvasive cardiac imaging. We planned to develop a technique to detect myocardial ischemia. After considering several alternatives, we decided to test the soluble tracer, rapid-clearance concept suggested by Sapirstein. Before trying this in humans, we thought it would be a good idea to work out the details in some animal studies. Zaret and I went to see the hospital commander, Monte Miller (who subsequently became surgeon general of the Air Force), to ask permission to do the animal studies. We explained the idea of injecting K-43 twice, once when the patient was at rest, and a second time, when the patient was exercising. Miller asked if the tracer had been used in safely in humans. We said yes. Miller said he did not want to have any animal studies done in the hospital, but he would let us test the idea in patients. We

arranged to get a small dose of K-43 shipped from Oak Ridge National Laboratory (Oak Ridge, Tennessee) to Travis so we could develop the imaging parameters with the rectilinear scanner. Harry Wells (chief technician in Nuclear Medicine) and I worked out the technical details of tracer injection and imaging. Based on the published data, we planned to continue exercise for at least 1 min after injection if possible to permit clearance of the tracer and uptake in the heart (Fig. 1). Based on our estimate of the dosimetry, we planned to inject 0.4 to 0.8 mCi of K-43. The images were recorded with a 5-in crystal (Picker Nuclear Division of the Picker Corporation, White Plains, New York), using a coarse focus collimator (Fig. 2). The pulse height analyzer was set to record photons between 340 and 700 keV, to capture about 197 photons/100 disintegrations. We planned to manually localize the center of the left ventricular myocardium by superimposing a chest film on the chest. This step would allow us to set the scan speed, based on the count rate from the myocardium. The scan speed was adjusted to produce an image with approximately 800 counts/cm^2 from the myocardium. In parallel

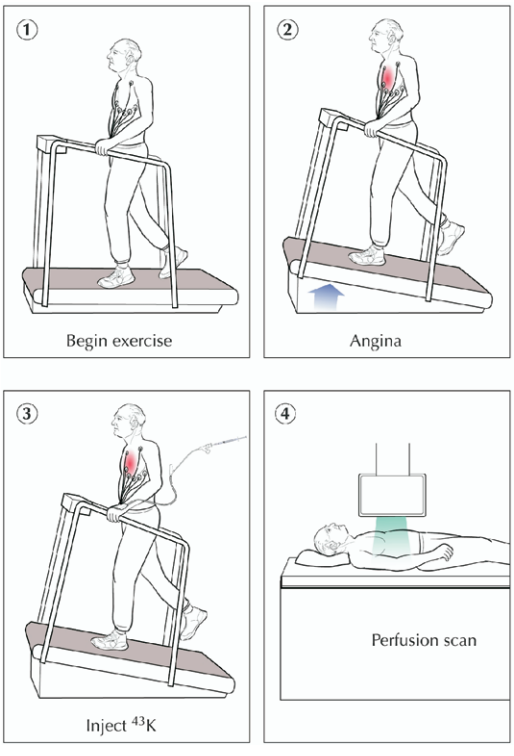

Figure 1. ECG and Patient Activity During the Stress Portion of a Myocardial Perfusion Study

At the start of exercise **(panel 1),** the electrocardiogram is normal. Further stress produces ischemia **(panel 2).** Exercise continues, the K-43 is injected, and exercise continues for at least 1 additional minute **(panel 3).** Following return to resting heart rate (no more than 5 min after tracer injection), the perfusion scan is recorded with the rectilinear scanner **(panel 4).** Modified from Zaret et al. Myocardial imaging for the noninvasive evaluation of regional perfusion at rest and after exercise. In: Strauss HW, Pitt B, James AE, editors. Cardiovascular Nuclear Medicine. St. Louis, MO: CV Mosby and Co, 1974:181–210. Figure illustrations by Rob Flewell.

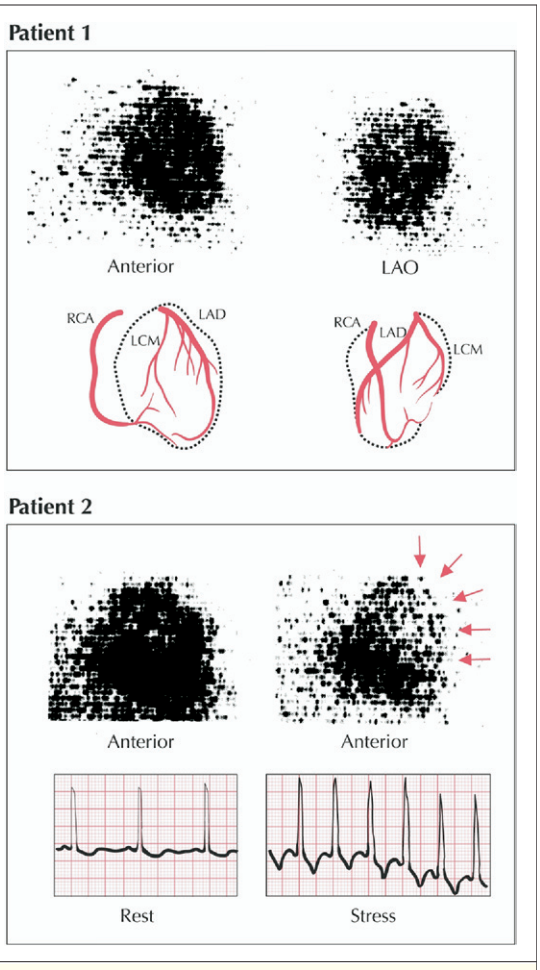

Figure 2. Normal and Abnormal Stress Myocardial Perfusion Scans in 2 Patients

(Top panel) Two views of a K-43 myocardial perfusion scan recorded with the rectilinear scanner in the anterior view **(left)** and left anterior oblique view (LAO, **right**) following injection of the tracer at stress. Diagrams of the coronary arteries superimposed on an outline of the scan **(bottom).** Note the uniformity of tracer uptake in the left ventricular myocardium in this normal subject. **(Bottom panel)** Anterior views of K-43 myocardial perfusion scan performed following tracer injection at rest **(left)** and during stress **(right)** with the corresponding electrocardiogram below each image. Note the marked decrease in tracer uptake in the anterior wall on the stress injected study **(arrows).** Modified from Zaret et al. (9). Figure illustrations by Rob Flewell.

with the development of the technical parameters, Zaret discussed the plans with Dan Flamm (Chief of Cardiology) and agreed to select a patient with chronic stable angina who was scheduled for coronary arteriography. When the patient agreed to the procedure, we scheduled another shipment of K-43 from Oak Ridge. Zaret supervised the stress test, and I did the injection and imaging. About 1 week later, Zaret and Flamm did the coronary arteriogram, and we knew the procedure worked (10,11).

In the 36 years since the initial stress perfusion scan was performed, there has been a steady evolution of instrumentation and radiopharmaceuticals. Today, myocardial perfusion images can be recorded with contemporaneous computed tomography (CT) using single-photon emission CT or positron emission tomography (PET)-CT instruments. Positron emission tomography is advantageous because it permits quantitation of absolute coronary blood flow and perfusion reserve. A state-of-the-art myocardial perfusion study and contemporaneous coronary CT angiography performed with PET-CT depicts regional myocardial perfusion, perfusion reserve, global and regional left ventricular function, coronary calcium score, and coronary anatomy. If further imaging with markers of inflammation is added, it may be possible to define vulnerable plaque.

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