dogs in 1966, and the feasibility of direct injection of radionuclide labeled particles into human hearts was demonstrated in 1970 using radioiodine. With the direct injection technique, virtually all radioactivity was localized in the heart and relative regional blood flow could be determined precisely. However, the inherent invasiveness and risks involved limited the application of direct injection to patients requiring cardiac catheterization.

Exercise-induced regional blood flow among patients with coronary artery disease using intravenously injected potassium-43 and rubidium-81 was demonstrated in the early 1970s. Thallium-199 and mixed thallium isotopes were used as imaging agents for heart muscle in the late 1960s under OHER support at the Franklin McLean Memorial Research Institute. Scientists at BNL developed the radiopharmaceutical production techniques for thallium-201 and demonstrated its use for heart imaging in the mid-1970s. This radionuclide is generated as the by-product of a process that starts with the bombardment by a particle accelerator of stable thallium-203 metal foils with protons.

The United States pharmaceutical industry invested between $20 and $25 million in developing the capacity to produce thallium-201. In 1981 about 370,000 thallium-201 scans were performed domestically. Thallium sales by the New England Nuclear Corporation alone increased from $14 million in 1979 to approximately $20 million in 1981. Worldwide thallium sales reached $28 million in 1980, up from $17 million in 1979.

Benefits The thallium-201 exercise testing has filled an important gap in the diagnosis of heart disease between electrocardiograph (EKG) exercise tests and the more invasive, risky, and expensive angiography using cardiac catheterization. This is especially true for females because false positive findings from exercise EKGs are much more frequent. Moreover, the inherent invasiveness, risk, complexity, and cost of angiography using cardiac catheterization weigh against its use to provide the necessary diagnostic information in a disease that affects over 500,000 Americans each year. The thallium examination not only extends benefits to those patients who would not be able to withstand cardiac catheterization, but it also results in better selection of those patients who require cardiac catheterization.

The introduction of a new technology into an already well-developed process produces an altered set of benefits and costs. For example, at the Johns Hopkins University Hospital between 1975 and 1977, 57 percent of the women who had cardiac catheterization to investigate chest pain showed no evidence of suspected coronary heart disease. In these cases, coronary angiography and simultaneous catheterization were required to be certain that the women did not have coronary heart disease. Today, nuclear cardiology procedures, chiefly thallium-201 exercise testing, have decreased this to less than 20 percent. Data from Johns Hopkins also indicate the increasing linkage of cardiac catheterization to cardiac surgery, with nuclear examinations solving nonsurgical diagnostic problems. The total National benefit has been estimated at over $70 million/year.

Technetium-99m for Diagnostic Scanning Technetium-99m is a radionuclide with a 6-hour half-life, favorable gamma-ray emissions, and no beta radiation. Depending on the chemical form, it concentrates in the liver and kidneys in a few minutes or in the skeleton in 2 to 3 hours after intravenous administration, thus allowing imaging with minimal patient radiation dose. Use of technetium-99m scans to examine prostate cancer patients identifies those—about 25 percent of the total—for whom expensive surgery or radiation therapy could be replaced by less expensive hormone therapies such as bilateral orchiectomy or exogeneous estrogens.

Technetium-99m is considered to have the best overall properties of currently available radionuclides for imaging with a scintillation camera (considering half-life of the radionuclide, patient radiation dose, gamma-ray energy, availability, and cost). Accordingly, it is used in over 80 percent of nuclear medicine examinations of the various body organs.

For routine diagnostic studies in adult patients, technetium-99m is administered intravenously in doses of 10 to 20 millicuries. Studies of the liver and kidney begin immediately. For the skeleton, imaging is usually performed 3 to 5 hours later.

It has been estimated that one in four patients hospitalized (out of 37 million admissions/year) in the United States received a technetium-99m-labeled compound as part of the diagnostic process. At least 6 million studies are performed annually. Industry is currently producing technetium-99m, with sales totaling $26 million/year.

History Artificially produced technetium is usually obtained from activated molybdenum-98. Technetium was discovered by Emilio Segre and Glenn Seaborg in 1938 at Berkeley, California, in the laboratory of Ernest Lawrence. Molybdenum-99 and its daughter nuclide, technetium-99m, were obtained as a result of the fission process.

For many years the medical possibilities of the use of technetium-99m were overlooked because of its relatively short half-life (6 hours). However, L. G. Stang, Jr. and Richards (working at BNL) invented the radionuclide generator, in which the user could chemically separate the technetium-99 radionuclide from its longer lived radioactive parent, molybdenum-99. This made possible the availability of the short-lived radionuclide at those sites where a reactor was not available.

Stang and Richards advertised both molybdenum-99 and technetium-99m for sale on the cover of the Brookhaven catalog of 1960. In 1961 Beck published a theoretical study demonstrating