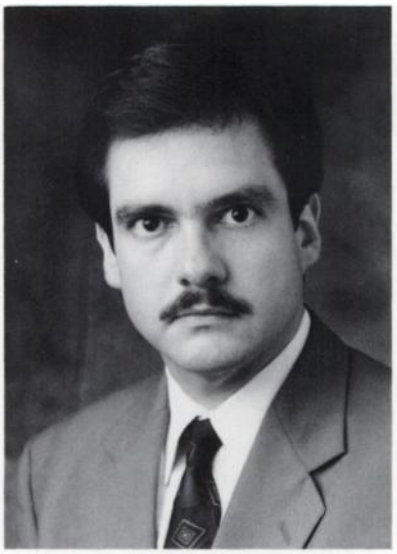
DUPONT AWARD

Two New Cardiovascular Research Fellowships Awarded to Investigators of PET and SPECT Diagnoses of Heart Disease

AN INVESTIGATOR PROPOSING to test the effectiveness of a PET stress test in diagnosing and predicting heart disease, and another who will correlate human heart metabolism with the uptake of a technetium-99m-labeled tracer to better define viable myocardium were announced as the recipients of the first annual Du Pont Pharma Cardiovascular Nuclear Medicine Research Grants at Annual Meeting of The Society of Nuclear Medicine in June.

The awardees, Luke Daley, MD, a fellow in cardiovascular medicine at the New England Medical Center in Boston, and Jorge Cuello, MD, a cardiology fellow at the University of Texas Health Sciences Center in San Antonio, were selected by the SNM Awards Committee. The two $25,000 grants, sponsored by Du Pont Merck Pharmaceutical Co., are intended to encourage physicians to enter the field of cardiovascular nuclear medicine and to support nuclear cardiology clinical research.



Jorge L. Cuello, MD

Luke Daley, MD

FDG-PET Stress Test

Dr. Cuello, working with Richard E. Stewart, MD, an assistant professor at UT, plans to assess the diagnostic efficacy and predictive value of PET scanning with fluorine-18-deoxyglucose, or FDG, injected during treadmill exercise stress in patients with chronic stable coronary artery disease. The test is designed to detect regional myocardial ischemia and give clues as to the likelihood of future problems, such as myocardial infarction or congestive heart failure.

The investigators believe that a test using a single tracer (FDG) injected at the peak of symptom-limited treadmill stress could be as accurate and possibly superior to exercise imaging protocols using a flow tracer like nitrogen-13 ammonia in combination with FDG.

A single-tracer PET stress test, if proven equivalent to dual tracer tests would have significant advantages. Patients would be subjected to less radiation and clinicians would save considerable time on each test.

Previous studies have shown that metabolic imaging with exercise stress may help the clinician define regional myocardial ischemia. But in almost all previous studies with FDG-PET, the metabolic tracer was administered during the recovery phase after peak exercise, partly because protocols involving a second flow tracer like ^{13}N ammonia necessitate injecting FDG after exercise.

Dr. Cuello says in his proposal that "the diagnostic and prognostic value of metabolic imaging utilizing maximal treadmill exercise and PET for detection of functionally significant coronary disease has not yet been fully defined." In his study, each of 25 enrolled patients will undergo a single tracer PET study and dual tracer PET study. All patients will be evaluated at 6 months and again at 12 months to assess for progression of anginal symptoms, the development of congestive heart failure, or the occurrence of myocardial infarction, bypass graft surgery, syncope, or death.

"We feel that this proposed research, carried out systematically in a clearly defined patient population at our institution, can significantly contribute to further characterizing this very important diagnostic imaging modality," Dr. Cuello says.

MIBI and Metabolism

By measuring the degree to which damaged myocardial tissue takes up

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Cardiology Awards

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technetium-99m sestamibi, cardiologists can predict to some extent whether revascularization surgery will improve ventricular dysfunction. But questions about the mechanisms and the accuracy of such predictions in human patients remain unanswered. Dr. Daley and colleagues, working in the nuclear cardiology laboratory directed by James E. Udelson, MD, at the New England Medical Center, propose to extend previous investigations of these questions by correlating single photon emission computed tomography imaging with regional tissue uptake of ^{99m}Tc-sestamibi, or MIBI, in patients with coronary artery disease.

The investigators will analyze the relation of MIBI uptake to metabolic parameters of viable myocardium and correlate the data with prospective assessments of the timing of improvement of myocardial tissue in patients following revascularization procedures.

Among other hypotheses, they expect that myocardium with mild to moderate reductions in MIBI activity will have relatively greater concentrations of ATP and creatine phosphate and will improve faster following surgery than segments with severe reductions of MIBI activity.

To assess uptake of MIBI and regional metabolism, investigators will take biopsies of scarred, ischemic, and adjacent non-ischemic myocardium prior to aortic cross-clamping. Divided into segments, the samples will be assayed for MIBI activity.

Metabolism will be assessed by assaying for lactate, ATP, creatine phosphate and glycogen. Global cardiac function will be assessed by hemodynamic measurements and measurements of cardiac extraction of lactate and oxygen. Recovery will be assessed by echocardiography.

In his proposal, Dr. Daley says the planned research will characterize, perhaps for the first time in humans, the correlation between quantitative imaging and regional tissue activity of ^{99m}Tc-sestamibi with regional myocardial metabolism and the extent of collateral flow, which previously has been explored only in animal models. He expects the work to corroborate the predictive value of ^{99m}Tc-MIBI SPECT imaging in assessing the recovery of function in dyssynergic myocardial segments following surgery and clarify the time course of recovery of regional ventricular function. ■

Therapy Award

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Cu-64-benzyl-TETA-MAb 1A3, developed against colorectal cancer is safe in humans and can be used with PET to detect very small colorectal tumors. The researchers tested the agent in ten patients with advanced colorectal cancer.

The antibody binds selectively to an antigen distributed abundantly on the surface of primary colon cancer cells that is rare or entirely absent in normal colon tissue. Previous studies have established that the antibody is internalized by colon cancer target cells, a mechanism which, Dr. Anderson points out, seems likely to increase the antibody's ability to kill cancer cells by bringing the radionuclide closer to the genetic material.

With the SNM/Medi-Physics fellowship, the researchers hope to establish whether ^{64}Cu-labeled monoclonal antibodies should be further developed for radioimmunotherapy in humans. "Getting this fellowship is really wonderful because it enables us to complete our cell studies and move on to the in vivo [animal] studies," says Dr. Anderson. "If the data looks good we hope to get a major NIH grant so we can move on to human clinical trials." ■

RIA

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surface and exciting a fluor.

For demonstration purposes, Dr. Jay used iodine-125 in his membrane-based assay, but he says the system should allow the use of higher energy beta emitters such as tritium, carbon-14, or sulfur-35. In the past, researchers assaying beta emitting radioisotopes like tritium had to add a "scintillation cocktail" containing dissolved fluors. Used cocktail contains both organic solvents and radioactive waste, which can be a disposal problem. With systems in which fluors are imbedded in beads, or now membranes, no mixed wastes are generated.

But with beads, Dr. Jay says, labeling with higher energy beta emitters is impractical. "You only want the stuff bound to beads to be detected," he says. "If the beta particles have a long enough range, particles from unbound radioligands might strike beads" and cause fluors to emit light. Dr. Jay is experimenting with membranes coated with films that are porous enough to allow molecules to penetrate into the membrane pores, but thick enough to shield fluors from beta particles emitted from unbound radioligands.

Another advantage of membranes is that they can be cast into many useful shapes and sizes, Dr. Jay says. His team is beginning to work on membranes attached to fiber-optic filaments, which could be used for remote assays of minute quantities of a radiochemical in body cavities, or outside of medicine in other industrial applications.

For now, he is in the process of patenting the membrane-based RIA technique. Experiments to optimize the membrane RIA system should be complete in about six months, but Dr. Jay says he hasn't begun efforts to commercialize the idea. "I tend to be an academic type," he says, adding that he's preoccupied with research and teaching graduate students.

The Berson-Yalow Award is named for the late Solomon A. Berson, MD and Rosalyn S. Yalow, who developed the RIA technique. The Society established the award in 1977, the year the Dr. Yalow received the Nobel Prize for Physiology or Medicine. ■