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Interim Report In Phase V Proposal: Incorporated Clinical Investigation Proposals #389 and #499, Noninvasive Assessment Of Coronary Artery Disease By Radioisotopic Techniques.

1. Investigators:

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2. Studies to date:

a. Through 31 March 1975, 407 potassium-43 studies and 301 rubidium-81 studies have been accomplished at rest or exercise on 393 patients. Six hundred fifty-six studies were accomplished using the rectilinear scanner and 52 with the scintillation camera. Patients have included those with the following diagnoses:

(1) Normal subjects
(2) Myocardial infarction
(3) Post myocardial infarction angina pectoris
(4) Angina pectoris without myocardial infarction
(5) False-positive and equivocal exercise ECG tests
(6) Cardiomyopathy and myocarditis
(7) Barlow's syndrome
(8) Conduction abnormalities including left bundle branch block, right bundle branch block, hemiblocks and atrioventricular blocks.
(9) Pre-excitation syndromes (WPW, LGL)
(10) Pericarditis and pancarditis
(11) Postoperative aortic coronary bypass graft evaluations in patients with and without postoperative symptoms.

3. Results and preliminary conclusions:

a. Although the rectilinear scanner remains our most frequently used instrument, rubidium-81 has allowed more extensive use of the scintillation camera, which has several potential advantages for investigative purposes. Our limited use of the scintillation camera results from the need for clinical data system. This attachment is available at all but a few of the medical facilities possessing scintillation cameras and permits greater diagnostic accuracy by providing contrast enhancement and greater objectivity by allowing coincidence counting in regions of interest. Should this piece of standard equipment be provided, we could change to the camera as our primary instrument which is more in keeping with recent developments in the techniques of myocardial imaging. For most clinical applications the rectilinear scanner has been satisfactory for the subjective evaluations as performed here for the past several years.

b. Because of imaging characteristics and reduced costs, as well as adaptability to the scintillation camera, we have converted 100% to use of rubidium-81, and since 15 November 1974, no longer image the myocardium with potassium-43. This has resulted in a reduction of 50% in radionuclide costs per study.

Thallium-201 has been considered for use, but its several disadvantages have offset some of its advantages over rubidium-81 and potassium-43, and its cost is three times that of rubidium-81, and represents a 50% increase in cost over potassium-43. In addition, we have received good information that a new radionuclide is to be expected within the next several months which could be incorporated into this protocol and would represent a significant improvement over all previous myocardial tracers.

c. Noninvasive myocardial imaging has continued to be both sensitive and specific in the diagnosis and the exclusion of atherosclerotic cardiovascular disease. To date we have found no false-positive exercise tests and false-negative exercise tests continue to occur in no more than 5% of cases. This 95% sensitivity exceeds the diagnostic accuracy of other noninvasive techniques and has proved to be a significant benefit in assessing the clinical significance of angiographically demonstrated obstructive lesions. As a result of this diagnostic accuracy, the need for coronary angiography in patients with atypical chest pain syndromes and suspected false positive exercise ECG tests has been dramatically reduced.

d. The diagnostic accuracy in anterior myocardial infarction is 98% (see paragraph f (1) below) and for inferior infarction is 80%. One hundred percent accuracy is the rule in true posterior myocardial infarction. This supplements our more recent work in recent infarct imaging with 99-technetium labeled stannous pyrophosphate in the accurate diagnosis of acute myocardial infarction, infarction localizing and sizing, as well as determination of extensions of existing infarctions. This has been of special benefit in evaluation of several patients with pancarditis, suspected of having suffered myocardial infarction because of ECG and enzyme changes. Another special use has been in the study of an unusual group of young patients with myocardial infarction who are apparently at low risk for subsequent coronary heart disease.

e. Our present protocol for regular followup of patients subjected to aortocoronary saphenous vein bypass grafting has been valuable in determining graft closure, intra-and postoperative infarctions and progression of disease in the native circulation. The necessity for repetitive postoperative coronary angiography has been obviated and important new data on the natural course of these patients is being established.

f. The number of patients with various ECG conduction disturbances at rest has now exceeded 40, with certain preliminary results evident:

(1) Patients with left bundle branch block and normal coronary arteries have resting anteroseptal scan defects which improve with exercise. This defect suggests a myocardial membrane abnormality as the cause of left bundle branch block in these patients.

(2) Patients with left bundle branch block and coronary artery disease have a resting anteroseptal defect which often worsens with exercise and if other than the left anterior descending coronary artery disease is present, the exercise image finds areas of abnormal tracer uptake in addition to that of the septum.

(3) Right bundle branch block unassociated with coronary artery disease and associated with normal rest and exercise images.

(4) Pre-excitation syndromes known to have a high incidence of exercise induced ST changes suggestive of myocardial ischemia manifests normal rest and exercise images in the absence of significant coronary artery disease.

g. In conjunction with protocol #500, the investigators have found that this technique is potentially capable of objectively evaluating the benefits of therapeutic agents used in the medical management of angina pectoris. This objectivity could be more refined and quantitative rather than qualitative data could be obtained if a clinical data processing system could be utilized as requested below.

4. Data presentation in conjunction with protocol #389 and #499:

a. Publications:

(1) H. William Strauss, Barry L. Zaret, Neil D. Martin, Harry P. Wells, Jr., and M.D. Flamm, Jr.: Noninvasive evaluation of regional myocardial perfusion with potassium-43: Technique in patients with exercise-induced transient myocardial ischemia. Radiology, Vol. 108, No. 1, Pages 85-90, July 1973.

(2) Barry L. Zaret, H. William Strauss, Neil D. Martin, Harry P. Wells, Jr., and M.D. Flamm, Jr.: Noninvasive regional myocardial perfusion with radioactive potassium: Study of patients at rest, with exercise and during angina pectoris. NEJM 288:809-812, April 19, 1973.

(3) Barry L. Zaret, Robert E. Stenson, Neil D. Martin, H. William Strauss, Harry P. Wells, Jr., Ronald L. McGowan, and M.D. Flamm, Jr.: Potassium-43 myocardial perfusion scanning for the noninvasive evaluation of patients with false-positive exercise tests. Circulation, Vol. XLVIII, pages 1234-1241, Dec 1973.

(4) Barry L. Zaret, Neil D. Martin, Ronald L. McGowan, H. William Strauss, Harry P. Wells, and M.D. Flamm, Jr.: Rest and exercise potassium-43 myocardial perfusion imaging for the noninvasive evaluation of aortocoronary bypass surgery. Circulation, Vol. XLIX, pages 688-695, April 1974.

(5) Neil D. Martin, Barry L. Zaret, Ronald L. McGowan, Harry P. Wells, Jr., and M.D. Flamm, Jr.: Rubidium-81, a new myocardial scanning agent: Noninvasive regional myocardial perfusion scans at rest and exercise, and comparison with potassium-43. Radiology, pages 631-636, June 1974.

(6) Martin, N.D., Zaret, B.L., Strauss, H.W., Wells, H.P., Albers, J.: Myocardial imaging using ^{43}K and the gamma camera. Radiology 112:446-448, Aug 1974.

(7) McGowan, R.L.: Radioisotope techniques for the evaluation of myocardial perfusion in patients with coronary artery disease. Medical Service Digest (in press) February 1975.

(8) McGowan, R.L., Martin, N.D., Zaret, B.L., Hall, R.R., and Flamm, M.D.: Rubidium-81 as an agent for noninvasive myocardial imaging at rest and exercise. Accepted for publication with revision, Circulation, February 1975.

b. Data from various segments of the potassium-43 and rubidium-81 myocardial imaging projects (Clinical Investigation Proposals #389 and #499) has been presented at the following meetings:

(1) Fourth Annual Meeting of the Northern and Southern California Chapters, Society of Nuclear Medicine, San Francisco, California, September 1972.

(2) 45th Annual Scientific Session, The American Heart Association, Dallas, Texas, November 1972.

(3) Western Section, American Federation of Clinical Research, Carmel, California, February 1973.

(4) Annual Scientific Session of the Society of Nuclear Medicine, Miami, Florida, June 1973.

(5) 46th Annual Scientific Session of the American Heart Association, Atlantic City, New Jersey, November, 1973.

(6) Advances in Heart Disease 1974, American College of Cardiology, 6th Annual Symposium On Clinical Cardiology, San Francisco, California, December 1973.

(7) Institute of Medical Research of Pacific Medical Center, San Francisco, California, January, 1974.

(8) Nuclear Medicine Institute, Cleveland, Ohio, January 1974.

(9) Seminars on "Myocardial Scanning With Potassium-43" have been presented by the David Grant USAF Medical Center staff at several university medical centers, both locally and throughout the country.

(10) 23rd Annual Scientific Session of the American College of Cardiology, New York City, February 1974.

(11) Society of Air Force Physicians (American College of Physicians Regional Meeting), March 1974.

(12) 47th Annual Scientific Session of the American Heart Association, Dallas, Texas, November 1974.

5. The research funds provided by the Office of the Surgeon General for fiscal year 1975 were sufficient, since a research grant from Merrell-National Laboratories paid for a large portion of the isotopes used in these protocols for that year. This funding has been terminated upon completion of Clinical Investigation protocol #500 and no supplemental funds are to be expected in fiscal year 1976. In spite of the ever improving clinical utility of these techniques, insufficient hospital funds can be budgeted for these investigative purposes, especially in the face of current cost reduction programs. If we are to continue to explore the diagnostic

potential of this procedure, USAF research funds for supplies and equipment are essential. In addition, as noted above, the state of the art has found a need for quantitative analysis of images to realize maximum diagnostic accuracy and scientific objectivity of acquired data. Qualitative studies with a rectilinear scanner, though still useful, are rapidly becoming antiquated. System upgrading is essential to further meaningful contributions from this USAF Medical Center in the field of Nuclear Cardiology. The following funding is requested for FY 1976:

a. Twelve millicuries of rubidium-81 per week for 50 weeks at a cost of $300.00 per week*. Cost: $15,000.00

*Assuming we continue six studies per week utilizing 2 mCi ^{81}Rb per study at $50.00 per study.

b. Expendable supplies that support the research studies included are Polaroid film and special recording tapes for the scintillation camera, ECG Cables and electrodes for the exercise treadmill, and publication expenses. Cost: $3000.00 *(See note in paragraph a.)

c. ADAC Clinical Data System with installation and warranty. Cost: $32,000.00**

7. The total research funds requested for clinical research proposal #389, combined with Clinical Research Proposal #499 for Fiscal Year 1976 is in the following categories:

a. Radionuclide rubidium-81	$15,000.00
b. Supplies and expense equipment	3,000.00
c. Investment equipment	32,000.00

** A discount of $3,000.00 can be obtained if this item is ordered prior to 1 Jun 1975, which unfortunately is still within FY 1975, and delivery would not be accomplished until FY 1976.

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