[redacted]

PROTOCOL SUMMARY

TITLE: IMAGING MYOCARDIAL BLOOD FLOW WITH N-13 AMMONIA

PRINCIPLE INVESTIGATOR: [redacted], MAJOR/SGHRI/567-8189

FACILITY: All the research positron emission tomography will be done at the research imaging center on the University of Texas Health Science Center-San Antonio Campus. Centers involved in this study are: Wilford Hall USAF Medical Center, Brooke Army Medical Center, Brooks Air Force Base, UTHSC-SA, and Audie Murphy Memorial Veterans Hospital.

1. PURPOSE SUMMARY: The validation of Positron Emission Tomography in the evaluation of patients with cardiac disease. Currently PET imaging has been shown in the literature to provide valuable information concerning myocardial perfusion and viability. The use of PET imaging overcomes some of the limitations of currently available modalities including single photon emission computed tomography. The use of perfusion imaging with N-13 ammonia will be evaluated within three arms of this protocol. The first AIM is to validate in our facility the sensitivity and specificity of N-13 Ammonia in the detection of coronary artery disease. The second AIM is to assess myocardial viability in patients with a) left ventricular dysfunction and contractile abnormalities b) Myocardial infarction post intervention with "incomplete" infarction and risk of extension. The third AIM of this study is to evaluate the use of perfusion imaging in conjunction with stress imaging for glucose utilization to evaluate ischemic changes. The second and third AIMS will utilize a dual tracer approach using N-13 ammonia and F-18 Fluorodeoxyglucose. Both tracers will be used under approved INDs and we will require signed informed consent to the use of each tracer prior to PET imaging.

Subject Population: 50 patients who are 18 years of age or older and are male or non-pregnant females. Patients will undergo routine cardiac examinations for the diagnosis of their coronary artery disease. If eligible, the patient will undergo PET imaging which will be accomplished on a single study day for patients in AIM 1 and AIM 3. The patients involved in AIM 2 are required to return in 6 months for follow-up as is standard of care and have a second PET scan performed to reassess

viability. This will be performed in a one day session as well. Volunteers will have stress perfusion imaging performed within two weeks of their PET scan and the PET scan session will be performed in a single day.

Radiation risk will be minimized by following the ALARA principle that the smallest dose will be used that will result in a statistically adequate study. The dose of a combined study of F-18 FDG and N-13 Ammonia is still well below the allowable radiation limit for volunteers as listed in the Federal Code for Radioactive Drug Research Committee. Even the additional dose from the Tc-99m Sestamibi for the volunteers stress perfusion imaging places the exposure at less than 1/4 the allowable dose. Neither N-13 ammonia nor F-18 FDG used in the amounts described has any known pharmacologic or toxic effects. No pregnant woman will be imaged and pregnancy tests will be performed on the day of PET imaging for all women of child bearing potential. Non-radiation risks include stress testing with either exercise or pharmacologic stress. The risks include chest discomfort, shortness of breath, nausea, ischemia and rarely death. The minor risks come from the placement of intravenous lines which may result in discomfort, bleeding or bruising. There is a small risk of claustrophobia which usually responds to reassurance. All procedures will be performed by appropriately trained personnel. The radioactivity will be used under the supervision of an approved handler.

Duration of the study is five years. The alternative to having PET imaging performed is to use conventional imaging to evaluate patients. This method is known to have false positive scans related to artifacts of tissue attenuation and false negative scans related to hibernating viable myocardium which appears to be scar tissue on conventional imaging.

2. INVESTIGATIONAL DRUG:
(a-c)
N-13 AMMONIA which will be used under IND #40,215 (PI: [redacted])
F-18 Fluorodeoxyglucose which will be used under IND#39,725 (PI: [redacted])

This will be manufactured on site as per the INDs at the Research Imaging Center facility at the University of Texas Health Science Center.

d. There are no known side effects of the proposed drugs N-13 Ammonia or F-18 FDG as per the USP:DI monograph

e. PATIENT SELECTION

GENERAL INCLUSION CRITERIA. Patients will be enrolled in this study after meeting these criteria:

a. Age: ≥ 18 years of age; males or non-pregnant females.

b. Patients with documentation of coronary artery anatomy by diagnostic coronary arteriography or volunteers with < 5% risk coronary artery disease by probability analysis.

c. Ability to give informed consent.

d. Patients:

1) Wall motion analysis by either 2-D echocardiography or radionuclide ventriculogram (for viability studies).

2) Perfusion imaging with stress* unless there is a clinical contraindication (i.e. unstable angina, (NYHA) Class IV CHF, uncontrolled complex arrythmia, hypertension or hypotension). This will be done in patients as part of their diagnostic evaluation.

3) Baseline electrocardiogram.

e. Volunteers:

1) < 5% risk of coronary artery disease.

2) Normal rest and stress* perfusion imaging.

3) Normal cardiac exam.

4) No history of diabetes or glucose intolerance.

5) Not involved in a study which has exposed them to radiation as a part of the protocol within the previous 12 months.

* Either symptom-limited treadmill or pharmacologic stimulation.

EXCLUSION CRITERIA.

a. Inability to cooperate with emission imaging.

b. Pregnancy.

c. Inability to provide informed consent.

d. Presence of abnormality on perfusion imaging in a volunteer.

e. Presence of glucose intolerance in a volunteer.

f. DOSAGE RATE SCHEDULE: The subject will receive a tracer dose of N-13 ammonia for each scan performed for perfusion imaging. The usual dose of N-13 Ammonia is 20-30 mCi. If a subject is to have a rest-stress perfusion scan this would result in a dose of 40-60 mCi of N-13 ammonia. If the subject is evaluated for myocardial viability, the subject will receive 20-30 mCi of N-13 ammonia and 5-10 mCi of F-18 FDG. For ischemia imaging the subject will have a rest-stress perfusion scan (40-

60 mCi) with a stress F-18 FDG scan (5-10 mCi). The only subjects required to have a reevaluation scan done are the myocardial viability group and they will have a rest N-13 perfusion scan and rest F-18 FDG scan on the initial and follow-up imaging sessions.

g. Modifications in treatment if side effects occur: As this is a non therapeutic study no modification of treatment is planned. In the event of an adverse reaction, emergency supplies and operating procedures are on site to support patients. If further care is needed the patient will be transferred via ambulance to the nearest facility.

h. Patients must have their diagnostic evaluations performed prior to becoming eligible for this protocol. Studies will be performed based on clinical indications for those procedures as would be considered standard of care. Once enrolled in the study, the patient will have a cardiac examination performed within one week of PET scanning and the PET scan will be scheduled on a single day session except for myocardial viability patients who will be reevaluated in six months with PET imaging again on a single session imaging procedure. Volunteers will have a stress perfusion study performed within two weeks of the PET imaging sessions.

3. Laboratory. radiology, or other support required: The department of Radiology is the source of this protocol and has the approval of the Research Imaging Center Director. The department of Cardiology has submitted a letter of support for their involvement in these studies.

4. The volunteers will have perfusion imaging performed with a dose of Tc-99m Sestamibi. Pharmacologic stress will be performed in subjects in conjunction with stress imaging with a dose of adenosine or persantine. Volunteers will be recruited form all participating centers.

5. Investigator categories: The principle investigator, Major [redacted] is on staff in the department of Radiology, as chief of Positron Emission Tomography. Associate Investigators: Dr. [redacted] of Cardiology is a staff member. The associate investigators from the department of Nuclear Medicine: Dr. [redacted], Dr. [redacted] and Dr. [redacted] are all currently on staff in the department of Radiology. Capt [redacted] is the staff radiopharmacist.

6. This protocol currently involves no gifts or grants. N-13 Ammonia and F-18 Fluorodeoxyglucose will be used in subjects and Tc-99m Sestamibi will be used in volunteers.

7. SIGNATURES:

[redacted], Maj, USAF, MC
Chief, Positron Emission Tomography Service

[redacted], Col, USAF, MC
Chairman, Department of Radiology