Protocol Title:	Assessment of Investigational Positron Emission Tomography and Post-Processing Procedures Performed as add-ons to Standard of Care Imaging
Protocol Date:	December 20, 2017
Research Project Number:	RP0689
Principal Investigator:	Michael V. Knopp, MD, PhD Professor of Radiology and Novartis Chair of Imaging Research Vice Chair of Research, Department of Radiology 395 West 12th Avenue, 4th Floor Columbus, OH 43210 Knopp.16@osu.edu Office: 614-293-9998 Fax: 614-293-9275

I. Objectives

The purpose of this study is to utilize investigational Positron Emission Tomography (PET) imaging acquisitions in addition to standard of care imaging:

1. To develop and refine PET post-processing acquisition procedures.
2. To generate preliminary and comparative imaging data for potential clinical trials.
3. To retrospectively evaluate standard of care PET imaging acquisitions by comparison with investigational PET imaging acquisitions.

II. Background and Rationale

PET imaging is increasingly being used as a diagnostic modality in cancer detection, staging and response assessment. Additionally, PET imaging is utilized in the detection and assessment of neurodegenerative or neurofunctional diseases, cardiovascular diseases as well as inflammatory processes. Constant advances in imaging acquisition and post-processing approaches enable a large variability of acquisition settings that can only be evaluated in real clinical situations with comparison to current standard of care imaging. We are proposing in this research only to use modified PET acquisition and post-processing approaches that do not lead to any additional radiation exposure or other risks to the patient.

III. Procedures

A. Research Design

The ***prospective portion*** of this study will utilize investigational PET acquisitions in addition to standard of care PET imaging to develop and optimize PET acquisition post-processing techniques as well as to generate preliminary and comparative data for potential clinical trials. These post- processing techniques include but are not limited to visual inspection of lesions, normal tissue, sentinel nodes and imaging artifacts, semi-quantitative analysis including the use of rating schemes, and using various published methods for image post-processing. The PET methodologies we plan to use as part of this study will allow us to obtain morphological, functional and molecular information.

Patients receiving a standard of care PET will be asked by study personnel if they are interested in undergoing additional investigational acquisitions before or after their standard of care imaging. If the patient agrees, he/she will remain on the same PET scanner for up to an additional 30 minutes while more images are obtained. Each patient will be imaged for no longer than 2 hours (standard of care imaging and additional investigational imaging). A routine clinical report will be generated for the clinically indicated PET by a nuclear medicine physician. Once this routine clinical PET scan is dictated and finalized, a study team member will obtain the report via IHIS and manually remove all identifiers. This report is being obtained for comparative purposes. All the data being compared will be coded using a unique study number.

Patients will be asked to provide study personnel with authorization to their medical records for follow-up on future related procedures as well as the current outcome of their imaging procedure. Additionally, participants will be asked if their imaging data from this study can be

used in a de-identified manner in the future for comparison with other imaging data or as preliminary data for the protocol development of clinical trials.

The ***retrospective portion*** of this study will involve the review of pre-existing PET imaging data collected from January 1, 2001 through December 5, 2017. The data to be reviewed/analyzed includes PET imaging data that has been previously collected in the course of standard clinical care. The PET imaging acquisitions obtained from the retrospective review will be utilized as a comparison to the investigational images obtained during the prospective portion of this study. The criteria that will be utilized to determine how the retrospective data will be utilized includes the following parameters: type of imaging study, diagnosis, age in decades, gender, and availability of data in the imaging archive.

B. Sample

The ***prospective portion*** of the study population will include 200 evaluable patients receiving a standard of care PET scan at The Ohio State University (OSU). Potential participants will be identified by study team members at the time of the patient's standard of care imaging procedure.

Inclusion Criteria:

- Male and female volunteers greater than or equal to 18 years of age.
- Patients receiving a standard of care PET scan at OSU.

Exclusion Criteria:

- Participants who are pregnant or lactating.
- Prisoners.
- Subjects incapable of giving informed written consent.

The ***retrospective portion*** of the study population will include up to 500 evaluable previously acquired and archived standard of care PET scans. The selection of the cases will be based on availability of a data set and match in disease or age or gender to cases of the prospective population. All retrospective datasets will be de-identified using an established approach that is detailed below.

Inclusion Criteria:

- Patients having receiving a standard of care PET scan that is archived at OSU.

C. Measurement / Instrumentation

Studies will be carried out using FDA approved PET scanners. PET is routinely used for clinical diagnostic studies.

D. Detailed study procedures

In the ***prospective portion***, written informed consent will be obtained from each participant prior to any protocol related activities in a private area with a study team member. As part of this procedure, study personnel will approach eligible participants and explain verbally and in writing the nature, duration, and purpose of the study as well as all associated risks and benefits. They will inform the participant that he/she may withdraw from the study at any time.

The patient will be given time to ask questions and review the consent form on their own. During the consent process, the patient will be asked if he/she 1) is willing to provide a release of their medical records pertaining to future procedures/injuries in the next 10 years and 2) is willing to allow their de-identified data to be used as comparison data in other research studies or as preliminary data for the development of clinical trials. If the patient agrees, he/she will have additional PET acquisitions before or after their standard of care PET imaging. The patient will remain on the same PET scanner for all acquisitions. The investigational imaging will take no longer than 30 minutes. Each patient will be imaged for no longer than 2 hours (standard of care imaging and additional investigational imaging).

In the ***retrospective portion*** of the study, all PET/CT imaging data will be downloaded from the imaging PET Grid or archive system to the dedicated imaging corelab service where the imaging data will then be de-identified and referenced only by a study ID number. We will retain / code the following information regarding the data so that we may use it comparatively with matched investigational PET imaging data: type of imaging, diagnosis, coded imaging exam date, gender, age in decades, weight in 20 pound increments, and height in feet increments (i.e. excluding inches).

The date of the exam will be coded to the first day of the quarter when the study was performed, except in cases where follow up studies are performed at a shorter time interval. If a shorter time interval exists, the date will be coded in relation to the baseline study that will be coded as the 1st of the quarter. For example, a baseline CT scan was performed on 10/5/2017 with a follow up on 10/7/2017, and the date coding would be 10/1/2017 for the baseline and 10/3/2017, preserving the relative time ratio within the quarter, but changing the date to a coded date.

Image Collection:

All patients in the prospective portion of this study will receive a standard of care PET. Patients will be asked to simply lie on the table of the PET system for the duration of clinically indicated PET. Subjects participating in the additional investigational imaging sequence will be asked to lie on the table for an additional 30 minutes before or after standard of care imaging while acquisitions are obtained. Participants will not participate in more than a total of 2 hours of imaging time per day because they will become uncomfortable lying still in one position and motion compromises the image quality.

Release of Medical Records:

The patient will be asked if he/she is interested in releasing their medical records for up to 10 years after their participation in this study in order to allow study personnel to track the current outcome and/or related procedures in the future. The patient can revoke their consent to this question at any time by contacting the Principal Investigator

Additionally, patients will be asked if their de-identified data can be used for other research studies as comparative or preliminary data. The patient can change their response to this question at any time by contacting the Principal Investigator.

E. Risks, Benefits, Safety and Confidentiality:

The patient will be injected with a radiopharmaceutical for the standard of care PET imaging procedure. The patient will not receive any additional radiation from the investigational imaging acquisitions obtained.

Risks:
There are no additional safety risks associated with the investigational PET imaging.

Benefits:
It is hoped that the information from this study will initiate changes in the field of view, changes related to table movement and changes due to detector settings such as energy window.

Safety Monitoring:
As part of the standard of care imaging procedure, safety monitoring measures on the patients. This will include the monitoring of the physiologic parameters that are deemed appropriate in the evaluation of potential risk during the acquisition process (electrocardiogram, respiration rate, core body temperature). These parameters are monitored to ensure that they do not approach potentially hazardous levels. The Principal Investigators or Co-Investigators are able to respond immediately to ensure the safety of the patients participating in the research study. The Principal and/or Co-Investigators or Key Personnel will be present at the time of all PET acquisitions to ensure this.

Patient participation maximum duration and frequency is defined by protocol as follows: Duration of data acquisition in the PET system per patient is limited to no more than 2 hours total per day consisting of one or more acquisitions.

In the event of any medical emergency, accident or trauma while the subject is in the laboratory, our contingency plans for emergency situations are as they would be for any medical facility and clinical magnetic resonance imaging facility. Our emergency protocol fully prepares us to provide access to emergency treatment for our patients, resuscitation, life support and medical care as needed.

Confidentiality of Records:
All paper and electronic data/information will be de-identified prior to any review or analysis. All paper documents will be stored in a locked file cabinet with limited access in the Department of Radiology at The Ohio State University. All electronic data obtained through PACS or IHIS will be stored in a de-identified manner on password protected servers with limited access in the Department of Radiology at The Ohio State University. In the Informed Consent, we are asking subjects for release of medical records for up to ten years, as well as the use of de-identified data for other future studies. This data will become part of the permanent archive of the Wright Center of Innovation and may be kept indefinitely. No individual identities will be used in any publications resulting from this study. If the subject has authorized the use of de-identified data for other research studies as comparative data, the de-identified data may be shared with collaborative investigators as well as research databases. The established processes to verify de-identified data will always be adhered to. Officials from examining bodies such as the U.S. Food and Drug Administration or NIH may inspect records pertaining to this study.

F. Internal Validity

Image data will be evaluated following standard published procedures. This includes but is not limited to visual evaluation of lesions, normal tissue, sentinel nodes and imaging artifacts, semi-quantitative analysis including the use of rating schemes, and using various published methods for image post-processing. This should ensure internal and external validity of the data and avoid study bias. Functional and molecular read outs will be established according to methodologies.

G. Data Analysis

As the purpose of this data is to demonstrate feasibility in real life applications, we do not intend to perform a statistical assessment beyond classifying the characteristics of pilot data and comparing observational trends either to the standard of care imaging data or other known reference data. For our purposes, imaging that presents lower imaging quality will not be pursued for further evaluation. Only images that suggest equivalent or improved image quality would be evaluated for the potential use of preliminary data toward a formal Phase I/II clinical trial.