B. TECHNICAL EXPERTISE

As an institutional research facility, the Institute for Innovation in Imaging is fortunate to have extensive technical expertise available to support the proposed instrument. Members of the i3 collectively have decades of experience in radiochemistry, GMP production and PET imaging. The broad range of radiochemistry and PET imaging expertise among the Institute faculty includes molecularly targeted radiotracers, synthesis with C- 11, F-18, Cu-64, Ga-68 and Zr-89, PET-CT and PET-MR imaging, image reconstruction, and quantification. The Institute also has significant experience in translating new PET tracers into clinical testing. From this experience, we are familiar with the technical challenges associated with radiotracer production of novel radiotracers. In addition to these technical domains, the i3 investigators and their collaborators from other MGH departments and other institutions (local as well as national and international) lead radiotracer and molecular probe development research programs.

The new i3 cGMP PET production facility will be run jointly with the Martinos Center PET production facility. Daily operation of this production instrument will be managed by the technical director and a dedicated technician, who will be responsible for maintenance, daily technical support, and run produciton. Scheduling and billing are handled through the Institute for Innovation in Imaging. Users must request accounts (funded, pilot, development) using an online form that are associated with a specific project/grant. Scheduling is handled by Ms. Dervin the administrative assistant. When users book production runs on the system, their usage is logged and they are billed accordingly upon use of the instrument as planned. Cancellations exceeding 4 times per year will be billed regardless of use to ensure the instrument is being used to full capacity. A training and orientation session will be mandatory for all researchers with need to use the cGMP facility to maximize communication and expections of the production runs and experiments that will be carried out.

Although the full range of expertise and resources at the Institute for Innovation in Imaging, the Martinos Center, the Center for Systems Biology and the Department of Radiology will indirectly support the proposed system, here we describe the roles of the key technical personnel who will directly support the Ga-68 automated radiotracer production system, filling critical roles for the initial set up, operation, maintenance, and quality control for this new system.

***Shared Instrument Director.*** The principle investigator, Peter Caravan, Ph.D., is Professor of Radiology at Massachusetts General Hospital and Harvard Medical School, Director of the Institute for Innovation in Imaging and faculty member at the Athinoula A. Martinos Center for Biomedical Imaging. He will be responsible for the scientific and administrative oversight of the proposed shared instrument, subject to the Scientific Management Committee. He will assure proper use and allocation of the instrument in accordance with Institute for Innovation in Imaging, MGH and federal policies. Dr. Caravan, along with the technical director, will oversee the siting and installation of the proposed instrument.

***Technical Director and Radiopharmacist.*** Philip Neilsen is a certified Nuclear Pharmacist. He will be responsible for the technical and administrative oversight of the proposed instrument. He will be responsible for maintaining logs of instrument use, performance and maintenance, for conducting regular quality control measures, and for ensuring that the instrument is maintained in proper working condition and utilized according to all federal codes. He is also responsible for the training and certification of users, and for maintaining compliance with institutional safety standards.

***Radiochemist.*** Mariane Le Fur, Ph.D. is a chemist with 7 years of experience in the design and synthesis of chelators for radiometals like Ga-68 and in developing and validating methodology for labeling tracers with radiometals. She will provide expertise in radiolabeling, automation, and in transferring early stage radiochemistry procedures to robust automated protocols. She will also provide expertise in troubleshooting labeling processes.

***Radiochemistry Technician.*** Danelia Bernales will be responsible for the day-to-day operation of the instrument. She will perform quality control checks, operate the instrument for radiolabeling, and perform the cleaning procedures.

***Administrative Assistant.*** The scheduling of the instrument will be performed in conjunction with the existing Martinos Center online scheduling system. Karen Dervin is the Martinos Center Core administrator who is responsible for core facility scheduling and billing, under the direction of the Center Core Director.

***Previously developed Ga-68 based probes that will made be available through this instrument.***

Approved for clinical imaging

68Ga-DOTATOC (somatostatin receptor, tumor staging)

68Ga-CBP8 (molecular probe to type I collagen: fibrosis, pancreatic cancer)

68Ga-PSMA (PSMA expression, prostate cancer)

68Ga-FBP8 (molecular probe to fibrin: thrombosis, multiple sclerosis)

Currently in translation

68Ga-Macrin (macrophage labeling probe: inflammation, immunotherapy monitoring, CVD)

68Ga-Allysine (fibrogenesis probe: IPF, NASH, heart failure)

68Ga-HER3 (HER3 protein expression: breast cancer)

68Ga-Granzyme B (granzyme B expression: immunotherapy treatment monitoring)

68Ga-RGD2 (anti-v3 integrin probe: activated hepatic stellate cells in liver fibrosis; cancer)