# PLEASE NOTE, T, F, SBIR/STTR, and OT grants are not allowed in the Major and Minor user section.

# C. Research Projects that require the Ga-68 automated radiolabeling system.

The proposed instrument will be housed in the new Institute for Innovation in Imaging cGMP PET production facility and utilized by researches from several departments within Massachusetts General Hospital. **Table 3** (**Section D**) summarizes major users of the proposed gallium radiochemistry production system and their estimated usage time (in %). We list 20 projects all funded by NIH. Of these, 16 are R01 grants, 1 R33, 1 U01, 1 K23 and 1 R44. We expect that this usage will vary as each project develops and as new funds are acquired for new projects.

Projects use of the proposed instrument can be divided into four broad categories:

1. Clinical Research: production of existing Ga-68 probes for use in human imaging experiments (Major Projects No. 1-6).
2. Development and translation of novel Ga-68 based imaging probes – including chemistry, preclinical studies and clinical translation (Major Projects No. 7-11 and Minor Projects No. 16, 19).
3. Availability of existing Ga-68 based probes to enable and accelerate preclinical research (Major Projects No. 12-15).
4. Acquisition of Ga-68 isotope for other research. (Minor Project No. 17, 18, 20).

Many of the projects that we have included in this proposal plan to develop new imaging tracers and tools that can significantly impact our understanding of both normal and abnormal pathologies, opening new pathways for treatment of such devastating conditions that including Alzheimer’s disease, stroke, diabetes and cancer. Finally, as a teaching institution, we believe that it is of paramount importance to acquaint the next generation of imaging scientists with the latest developments in clinically focused PET imaging and therapy development by providing access to systems that, in combination with other imaging modalities, will enhance teaching potential. The projects below are presented in the order of **Table 3.**

# MAJOR RESERCH PROJECTS

**Project 01:** Multimodal MR-PET Machine Learning Approaches For Primary Prostate Cancer Characterization

**PHS Grant Number**: R01CA218187 (02/21/2018-01/31/2023

**Investigator**: Ciprian Catana, MD, PhD.

**Project Category: 1** - Clinical production for use in human imaging experiments.

1. **Goals.** Prostate cancer (PCa) is the most diagnosed form of non-cutaneous cancer in US men. The selection of patients who require immediate treatment from those suitable for active surveillance currently relies on non-specific and inaccurate measurements. A method that allows clinicians to more confidently discriminate clinically relevant from non-life-threatening tumors is needed to improve patient management. We hypothesize that attenuation maps as accurate as those obtained using a 511 keV transmission source – the true gold standard for PET AC – will be obtained. We hypothesize that the diagnostic accuracy of this approach will be superior to that offered by the stand-alone modalities. We hypothesize that machine learning approaches will achieve a higher predictive accuracy when applied to data acquired simultaneously than sequentially.

**Aim 1.** Develop and validate an MR-based approach for obtaining quantitatively accurate PET data. **Aim 2.** Identify the multimodal radiomics model that most accurately predicts PCa aggressiveness. **Aim 3.** Evaluate radiomics and deep learning approaches for predicting pPCa aggressiveness.

1. **Background and Significance.** Multiparametric magnetic resonance imaging (mpMRI) is the preferred non-invasive imaging modality for characterizing primary PCa. However, its accuracy for detecting clinically significant PCa is variable. We propose to address this limitation by combining mpMRI with positron emission tomography (PET) with a PCa-specific radiotracer and using advanced multimodal machine learning models (i.e. radiomics and deep learning) to characterize tumor aggressiveness based on the imaging data.

Recently, scanners capable of simultaneous PET and MR data acquisition in human subjects have become commercially available. An integrated MR-PET scanner is the ideal tool for comparing MR and PET derived image features to identify those that provide complementary information and build a hybrid PET-mpMRI model that most accurately identifies clinically significant tumors. While this novel technology allows the acquisition of perfectly coregistered complementary anatomical, functional and metabolic data in a single imaging session, a new challenge needs to first be addressed to obtain quantitatively accurate PET data. In an integrated MR-PET scanner, the information needed for PET attenuation correction (AC) has to be derived from the MR data and the methods currently available for this task are inadequate for advanced quantitative studies.

1. **Preliminary Results.** We have formed an academic-industrial partnership to accelerate the translation of multimodal MR-PET machine learning approaches into PCa research and clinical applications by addressing the AC challenge and validating machine learning models for detecting clinically significant disease against gold standard histopathology in patients undergoing radical prostatectomy.
2. **Future Experimental Plan and Need for the Proposed Instrument**. The Ga-68 automated radiotracer production system is essential for the success of our project in which we proposed to use [68Ga]-PSMA, an agent that exhibits high specificity for prostate cancer cells given their significantly increased expression of PSMA. Previous studies have shown that adding the PET's prostate cancer-specific information to structural/functional MRI may improve the diagnostic accuracy of MRI in this primary prostate cancer patients. Our goal is to combine [68Ga]-PSMA PET and multiparametric MR data to improve the characterization of clinically significant primary prostate cancer. We will utilize the proposed equipment to produce [68Ga]-PSMA for preclinical and human clinical imaging experiments. We hypothesize that a machine learning approach applied to multimodal MR-PET images that capture morphological, functional and molecular changes in prostate cancer will result in a method with enhanced diagnostic performance. The dedicated Ga-68 automated radiotracer production system will allow essentially on-demand cGMP production of [68Ga]-PSMA which will accelerate my research by increasing the number of days at which it is possible to scan subjects and thus make patient recruitment easier.