

Setting Up a PET Imaging Lab



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The Role of PET In Preclinical Imaging

Molecular imaging enables scientists to non-invasively visualize, characterize and quantify normal and pathologic processes *in vivo* at the cellular and subcellular level. Positron-emission tomography (PET) is a molecular imaging technology which utilizes radionuclides to deliver high spatial and temporal resolution data. The G-Platform, G4 PET/X-ray and G8 PET/CT systems, removes many of the technical hurdles for the scientist that may want to incorporate PET imaging into their research lab. However, there are some regulatory and safety requirements one must satisfy before the lab is approved to perform PET imaging studies. This white paper will outline many of the key regulatory and safety considerations, as well as providing a list of materials to consider purchasing to outfit a preclinical PET imaging facility.

Regulatory Considerations

Each country and state may have slightly different regulations, but there are some common considerations when applying for approval to use PET radioisotopes in preclinical imaging.

In the United States, the US Nuclear Regulatory Commission oversees the use of radioisotopes in academic settings. Most academic medical centers and universities have a broad scope license. This license covers a wide range of applications and isotopes. In many academic settings, the investigator's lab submits an application to use an isotope under the broad scope license.

There are several things to consider when submitting an application.

1. What isotopes will be used?
2. What will these isotopes be being used for?
3. What doses of isotope will be used and how much activity needs to be on-site, both for experiments and decay storage?

There is a wide range of PET isotopes available. Initially, utilizing robust imaging methods with PET agents like ^{18}F -Fluorodeoxyglucose (FDG) is a good starting point. FDG is a glucose analog and reports on metabolic activity *in vivo*. Fluorine-18 is often chosen as a PET isotope due to its relatively short half-life. Many academic medical centers have a cyclotron on site that produces ^{18}F for clinical applications, and preclinical researchers can often obtain ^{18}F and FDG from the radiopharmacy. If this is not possible, large radiopharmacies can deliver ^{18}F to the lab.

Recently, the field of immunoPET has expanded, and isotopes with longer half-lives are desirable because they can more closely fit the blood half-life of antibodies and antibody fragments. The isotope 89-Zirconium (^{89}Zr) has a half-life of approximately three days. This decay time coincides with the blood half-life of antibodies. PerkinElmer is a leading provider of ^{89}Zr .

Isotope	Half-life	Probes/Applications
^{18}F (Fluorine)	1.8 hours	FDG, FLT
^{89}Zr (Zirconium)	3.3 days	Label antibodies
^{64}Cu (Copper)	12 hours	Label antibodies
^{11}C (Carbon)	20 minutes	Label small bioactive organic molecules
^{124}I (Iodine)	4.2 days	In vivo pharmacological studies
^{68}Ga (Gallium)	1.1 hours	Label large biomolecules

Laboratory Safety Considerations

The general practices of ALARA (As Low As Reasonably Achievable) should be followed in the laboratory. This means making sure all steps are taken to keep the exposure to the researcher as low as reasonably achievable. This can be accomplished through a series of procedures outlined here.

Limiting Access

One of the easiest ways to reduce radiation exposure to non-PET scientists is to limit access to isotopes through the use of dedicated rooms and card readers. While the G4 and G8 PET systems are designed to be installed on any laboratory bench space, controlling access to the source of the isotopes will ensure greater compliance and reduce unexpected exposure. Additionally, only specific researchers that have received the proper training in handling and injecting radioisotopes should be approved to perform PET imaging studies.



Figure 1. The lead L-block shield weighs 195 pounds, and the 3-walled enclosure weighs 475 pounds, so care should be taken to ensure that the table/bench that the dosing station is installed on can support this weight.

Shielding

Once inside the laboratory, it is important to reduce potential exposure to radioactivity. ALARA regulations are best accomplished by using time, distance and shielding when handling radioactive isotopes. First, limit the amount of time handling the isotope. After injecting the isotope, quickly and properly discard the empty syringe into the proper radioactive waste container. Second, the radiation worker should maximize their distance from the animal being imaged. Third, the radiation worker should place all radioactive isotopes behind a lead barrier. Lead shielding is an important tool in achieving this. Due to the high energy of many PET isotopes, 2" thick lead is recommended.

Dosing Station

The area in the PET imaging lab that will have the highest radiation exposure potential is the dosing station. A lead enclosure to store radioactivity doses behind, as well as dose out aliquots, is required. Due to the high energy of PET isotopes, 2" thick lead should be used. Additionally, a leaded glass view window reduces exposure to the investigators eyes while aliquoting the isotopes.

Dose Calibrator

Dose calibrators are required equipment to obtain quantitative PET results. To know what percent of the injected dose was delivered to the target the researcher needs to know what the initial injected dose was.

Dosimetry and Monitoring

To track how much radiation exposure a user is exposed to they must utilize dosimetry when working with isotopes. For PET imaging it is important to monitor both the whole body exposure with badge dosimeters as well as exposure to the hands because of the high energy of PET isotopes.

Ring dosimeters should be worn when working in the PET laboratory. Initially it may be requested that a ring dosimeter be worn on both hands.

Waste storage

Many facilities will utilize a decay in store procedure for nuclear medical waste where waste is maintained on site until it is no longer radioactive, then disposed of through normal laboratory waste streams. For preclinical PET imaging in small animal models there are few considerations. The first is related to the isotopes that are chosen and the time required to store the waste until it



Figure 2. A dose calibrator enables the investigator to accurately measure injected dose to obtain quantified PET data.

has decayed to background, typically 10 half-lives. The second is the volume of studies that will be carried out. Carcasses and experimental waste, including needles, syringes and surgical supply waste also need to be stored until decayed.

Following the imaging sessions, waste should be bagged, tagged with a label that indicates the date and amount of activity used, and then placed in the correct waste receptacle. Before disposing the decayed waste in normal waste streams, the waste must be surveyed to ensure it has decayed to background levels.

Survey the Work Area

To ensure that the researcher is working in a clean environment, surveys should be performed prior to initiating any work in an area, as well as at the end of any experiments. If the researcher leaves the area during the experiment a survey should also be performed and documented.

Designing the Workflow

It is important that the imaging lab is laid out in such a way that the imaging workflow is easy to follow. When the dose of isotope arrives to the lab, it should be placed behind the thickly shielded dosing station. An aliquot of the isotope can be drawn up and injected into the mouse, which will then be placed in a cage behind the cage storage area to await imaging. Following the imaging session, the mouse may be placed back behind the cage storage area if additional imaging is required, or it may be euthanized. Waste is collected in isotope specific waste streams to ensure proper decay times are adhered to. Once the waste has been deemed to no longer be radioactive (generally after 10 half-lives), it should be surveyed and disposed of in the proper waste stream (chemical waste, solid waste or biohazardous waste).

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Figure 3. The G4 and G8 systems can be installed on an existing lab bench and comes with anesthesia and imaging chambers, a full PET lab in a small footprint.

Training

All researchers working with PET isotopes are required to participate in a PET training program. Topics may vary depending on the institutional requirements, but in general, some of the topics covered will include:

- PET radioisotope (i.e. ^{18}F) radiological properties
- Survey instrument use
- Contamination control and monitoring practices
- Radiation Safety and ALARA Practices
- Emergency procedures
- Proper injection techniques for administering agents in mice/rats
- Disposal practices for animal waste and animals

Other Items

There are a few other things to keep in mind when setting up a preclinical PET imaging lab:

- Imaging Lab location, keeping in mind adjacent spaces
- IACUC approvals in place
- Surgery and injection supplies available
- Long term housing of animals for longitudinal imaging
- Logistics for ordering and receiving radioisotopes
- Documentation procedures for receipt, use and disposal of radioactive waste

Summary

With the G-Platform, integrating PET into current pre-clinical molecular imaging workflows that may include optical imaging, MR and microCT no longer requires extensive (and expensive) laboratory renovations. The high PET sensitivity lowers the amount of radioactivity required, thus reducing exposure levels to the researcher, as well as the research subject. Installing proper shielding and ensuring regulatory approvals are obtained means the researcher can start acquiring PET data on the day of system installation.

