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We use this protocol and it's working

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Abstract

Summary:

The Center for Molecular and Genomic Imaging (CMGI) provides small animal imaging services for preclinical research. Contrast agents are a prerequisite for scientifically useful imaging studies involving microPET and microSPECT. In some studies, a contrast agent is also necessary for microCT imaging studies. Contrast agents include iodine-based compounds for x-ray computed tomography (CT), gadolinium for magnetic resonance imaging (MRI), and radioactive tracers for positron emission tomography (PET) and single photon emission computed tomography (SPECT).

Materials

MATERIALS

Fenestra **ART Inc.**

Reagents and Materials:

- 28 ga or 30 ga needle
- PE10 or MicroRenathane tubing
- Isoflurane, Ketamine/Xylazine, or Pentobarbital
- Gadolinium
- Radiotracer
- Fenestra

Troubleshooting

Safety warnings

WARNING HAZARDOUS CONDITION WARNED AGAINST.
Isoflurane must be used in a well-ventilated room from which there is no recirculation of exhaust air and will be used with the benefit of a scavenging/ventilation mechanism that eliminates inhalation exposure

All blood components and biological materials should be handled as potentially hazardous. Follow universal precautions established by CDC when handling and disposing of infectious agents.

1 **Micro- PET, CT, SPECT imaging procedures**

1. For some radiotracers, mice or rats will be fasted (water unrestricted) for up to 20 hours to improve radiotracer uptake.

2. Various radiotracers (see Radiotracer list below) are available for micro-PET (mPET) imaging in small animals. Trace amounts (<1 mCi, mice; <4 mCi, rats) of a short-lived radioisotope will be administered by iv, ip or sc injection prior to imaging. Only micro- to nanogram doses of radiotracer will be utilized, which will not cause any pharmacologic effect.

a. In some cases, a small catheter (mouse or rat: 28 ga or 30 ga needle on PE10 or MicroRenathane tubing; rat: commercially available 22 or 24 ga iv catheter) will be temporarily inserted into the tail vein of the conscious or anesthetized animal for isotope injection.

b. For conscious animal injection: animals are briefly restrained in a commercial restrainer for catheter placement or tail vein injection of radiotracer. (Tail may be immersed in warm water for 30-60 seconds to increase vasodilation of the tail vein.)

c. Prior to catheter insertion, the tail is cleaned with an alcohol wipe and the catheter, filled with heparinized saline, is inserted into the tail vein.

d. A needle/syringe or catheter plug is inserted into the end of the catheter until the radiotracer is ready to be injected. The isotope syringe is held in a syringe shield whenever possible to minimize radiation dose to personnel. The radiotracer uptake period prior to imaging is typically 0.5 hr, but may last from 0-2 hr depending on the protocol. During this time the animal may be continuously anesthetized or conscious. If the animal is anesthetized during this time, it is kept warm by a heat lamp or other heating device (e.g., Deltaphase pads).

3. For image acquisition, the animal will be placed on plastic-backed absorbent paper to contain any excreted urine, and imaged by the microPET or microSPECT scanner (typically for 10 min to 2 hr) or microCT (typically for 10-30 min).

4. In some longitudinal studies, animals may be rescanned several times per week for several weeks. For some studies, two animals may be imaged simultaneously, each with its own nose cone for anesthetic delivery. For microCT imaging, x-ray contrast agents may be utilized to highlight certain soft tissue features, or to visualize the vascular system. The microCT contrast agent, Fenestra, is typical dosed at 0.2 ml/20 g in the

mouse, and 5-10 ml/kg in the rat. Manufacturer recommendations will be followed for contrast agent injection within the allowable volume of injection.

5. In some cases, 2-3 small, low-radioactivity fiducial markers may be affixed to the fur or skin of the animal. These markers are visible on PET, MRIs and CT scans, and allow coregistration of the multimodal images, thereby providing the anatomical information afforded by CT or MRI imaging to better interpret the PET image.

a. If attached to the skin, the animal will be shaved in the regions where the markers will be attached, and a commercial hair removal cream may be applied briefly to remove stubble if necessary. The markers will either be taped in place or, if the animal is to be euthanized after the scan, may be glued to the skin.

2 **MRI imaging procedures**

1. Mice or rats will be anesthetized, placed inside the MRI scanner and imaged typically for a period of up to 1 hour. Animals are warmed by the imaging bed to maintain body temperature.

2. Contrast agents (e.g., gadolinium, paramagnetic gadolinium-containing liposomes, superparamagnetic iron oxide nanoparticles) may be utilized to highlight certain soft-tissue features, and these would be typically be injected iv unless there is difficulty with iv injection and it is known that the agent can be absorbed by ip injection.

3 **Optical imaging procedures**

1. For optical imaging, anesthetized animals may be imaged in a Xenogen IVIS system, typically for bioluminescence imaging, or a Maestro 2 system, typically for fluorescence imaging.

2. In some cases, animals will be shaved in the regions where signal is anticipated and a commercial hair removal cream may be applied briefly to remove stubble in order to optimize transmission ofthe light signal emitted from within the animal’s body.

3. For bioluminescence imaging, anesthetized animals carrying a bioluminescent reporter gene are injected ip or iv with the substrate for luciferase (luciferin, 150 mg/kg iv/ip or coelenterazine, 3 mg/kg iv/ip). Animals are placed on a warmed surface in a light-tight box (IVIS imaging chamber) and imaged with a sensitive CCD camera for typically 20 min or less.

4. For fluorescence imaging, anesthetized animals are injected (iv, ip, sc, or im) with a small quantity of fluorescently-labeled murine antibody, fluorescently-labeled microspheres, or red/near-infrared emitting optical contrast agent. Animals are placed on

a warmed surface in a light-tight box and the fluorescent light is imaged with a sensitive CCD camera for periods typically ranging from seconds up to sixty minutes.

a. Alternatively, animals or cells transfected to produce fluorescent proteins can be used.

4 **Radiotracers:**

PET: ^{18}F-fluorodeoxyglucose (FDG), ^{18}F-fluorothymidine (FLT), ^{18}F-fluoromisonidazole (FMISO), ^{18}F- penciclovir analog (FHBG), ^{18}F-paclitaxel, or ^{18}F-labeled peptides, antibodies, microspheres, acoustically active liposomes, microbubbles or cells; ^{64}Cu-PTSM, ^{64}Cu -ATSM, or ^{64}Cu-labeled microspheres, microbubbles, liposomes, peptides, antibodies or cells; ^{11}C-raclopride, ^{11}C-SCH23390, ^{11}C-PK11195, or other ^{11}C-labeled compounds; ^{89}Zr-labeled proteins, peptides, antibodies, microbubbles, liposomes or cells; ^{90}Y-labeled compounds, microbubbles, liposomes or cells.

SPECT: ^{99m}Tc, ^{111}In, ^{123}I, ^{125}I and compounds labeled with these radioisotopes may be utilized.