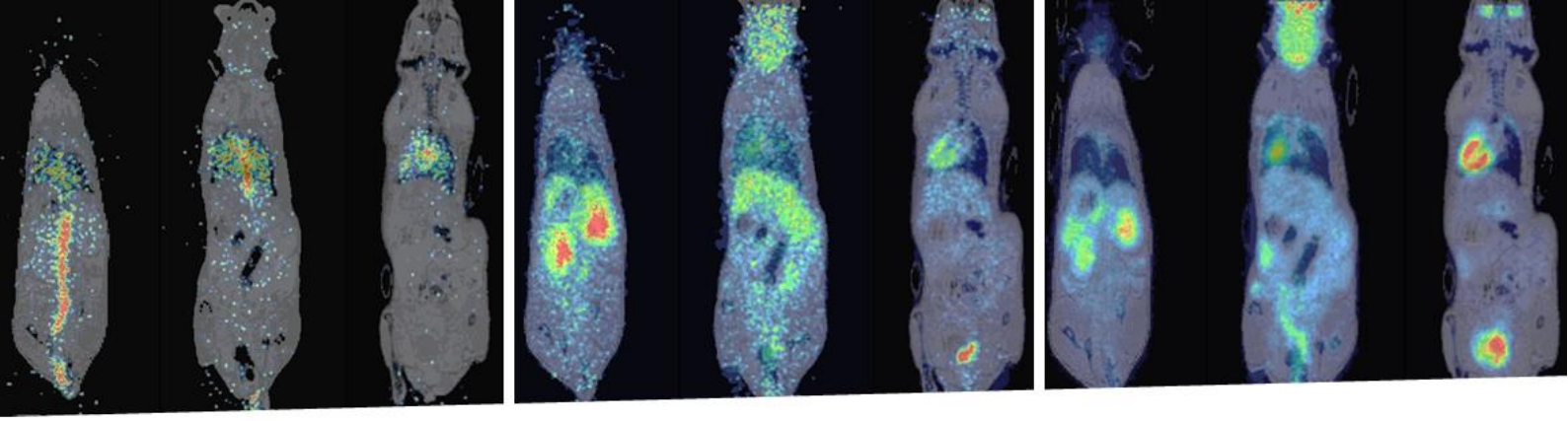

Method Note

Simultaneous Mouse Dynamic PET/MR

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Innovation with Integrity

Introduction

Dynamic PET imaging in preclinical research provides real-time, quantitative data on tracer kinetics, metabolism, and drug-target interactions. It enhances accuracy in kinetic modeling, biomarker validation, and therapy evaluation, making it a very powerful tool for drug development and disease characterization. In combination with PET, MRI enhances PET by providing high-resolution anatomical detail with rich soft tissue contrast and resolution. This method note provides detailed instructions for conducting simultaneous single mouse dynamic PET/MRI imaging in a Bruker system. It covers the necessary materials, equipment, animal handling techniques and procedures to ensure accurate and reliable results. Researchers will find this guide useful for setting up and executing their imaging studies, as well as for finding tips to effectively overcome common issues.

Materials & Equipment

MRI: Bruker AV4 70/30 BioSpec comprising a 7T, 300 mm bore magnet with B-GA20S HP gradients and operating with Paravision 360 v3.5. PET: The PET images are acquired on a 3-ring PET insert with an axial FOV of 150 mm, transaxial FOV of 80 mm. RF coil: 72 mm PET Optimized volume coil. Mouse Cradle: MMPF medium mouse cradle. Start heating ~30 min before the first animal to allow cradle temperature to stabilize. Place a block of foam over the height adjustment knob on the Autopac with a "bluey" or bench role to the start of the animal cradle. The syringes with activity can then be placed on the block.

FIGURE 1. Bore of magnet showing the animal transport system known as Autopac and the MMPF cradle.

Animal Preparation

Cannula: custom cannulas are prepared using 0.010" × 0.030" OD Tygon microbore tubing and a pulled 30-gauge needle inserted in one end and intact 30G needle inserted in the other end. Tubing length of 75 mm allows the attached syringe to be just outside the bore of the magnet. Total dead volume of the cannula is ~90 µl, comprising ~5 µl/10 cm of tubing and ~50 µl in the needle connector void. The cannula is filled with heparinized saline with a 1 ml syringe attached containing ~0.5 ml heparinized saline.

Tail vein cannulation: The animal is anesthetized with ~2% isoflurane in 100% oxygen on a heating pad and glove with warm/hot water placed on the tail. The tail vein is cannulated with movement of blood into the cannula confirmed with gentle pressure on the vein above the cannula. The needle is glued with super glue and then tape is place around the tip of the tail and cannula to limit movement of the cannula relative to the tail.

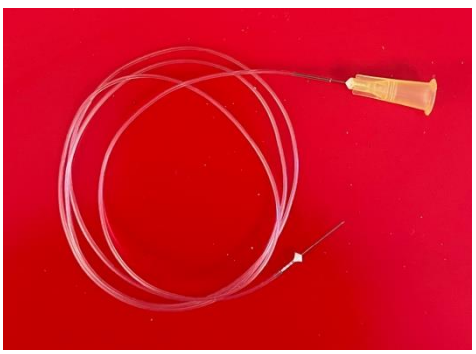

FIGURE 2. Needle, cannula prepared to use with syringe.

Dose preparation

Prepare the dose in 250 µl and draw up into a 1 ml Luer lock syringe. This results in ~200 µl being pushed due to the 50 µl dead space in the tip of the syringe. If "zero dead space" syringes are used, prepare 200µl volume. The total syringe activity for a mouse should be ~15 MBq. 50 µm Gadovist can be included if estimation of blood brain integrity is required. Connect the dose syringe to the cannula, ensuring there are no bubbles.

Animal placement

1. Place the animal in supine position in the cradle, connected to the tooth bar. Gently tape the respiratory pad over the abdomen and ensure there is a good respiratory signal. Gently tape the front and rear paws down to reduce movement. Close the top of the animal cradle.

2. Turn on the laser and move the animal to the required position and then turn off the laser.

3. Record the value of the laser, something like 750 mm.

4. Select “work” to move the animal to the imaging location.

Study Registration

1. Register the details of the animal, including date of birth, weight and the correct animal cradle.

2. Select headfirst supine for location.

3. Make sure MRI and PET are both selected.

4. Select the correct protocol e.g., UQ mouse > body > 72mmPO_liver > localizer. In the PET tab, make sure the correct isotope is selected, insert 10MBq and NOW for the calibration time.

5. Select create and scan.

Imaging

1. The localizer should be in the instruction list.

2. Tuning and matching: Select the localizer and then select wobble and then setup. Adjust tune and matching if required.

3. Run Localizer

4. T2-cor and position on the localizer images. In the adjustments run the Bo Map. (this must be performed before the PET starts).

5. T2-sag and T2-tra images.

6. MGE_2echo_cor_NR5 and position the 6 slices so the top slice includes the brain and kidneys, and the bottom slice is through the heart. Position the MAPSHIM region over the mouse where required. Run with 5 repeats. Inspect the images, view the 2-5 repeats.

7. T2_cor_5_slices right click adjustments > geometry to position the slices in the same location. These images are better quality image to position ROIs for analysis.

8. MGE_2 echo_cor_NR100 duplicate the MGE_2echo sequence and change the number of repeats to 100, ~12 min of total acquisition time. Apply but do not start.

9. PET_30min copy across and apply.

10. Select the MGE_2echo_cor_NR100 and continue. Both the MR and PET sequences should start. following ~1.5 minutes of acquisition, go into the MR-PET and push the dose into the animal. The PET activity trace should rapidly increase, and the live dynamic scan should show uptake into the animal.

11. MGE_T2star_map – copy geometry from MGE_2echo_cor_NR5. Apply.

12. T15500_T2map15 - copy geometry from MGE_2echo_cor_NR5. Apply.

13. FISP_3D_sag – position to cover the whole mouse and apply.

At the end of the imaging remove the animal. Remove the cannula and syringe and measure the activity. This is used to calculate the actual activity injected into the animal.

Image Reconstruction

1. Determine to offset required for the attenuation map. The cradle position divided by 10 (750/10 = 75). Then 440 – 75 = 365

2. FISP: Gradient linearity correction: P2 – select P1>right click>Create Image Series> MRI data Reconstruction>select Prototype Reconstruction>select Gradient Linear Correction. Rename to include GLC.

3. Attenuation map: P3 – select P2 > Create image series > select attenuation map and insert 365 into the Reference position [mm], ensure include study cradle is selected and is the correct cradle. Select the + and select the correct RF coil. Execute.

4. View the attenuation map and ensure the nose of the mouse is in the nose cone of the cradle. If not, the offset value is not correct.

5. PET: Determine the actual start time of the PET scan using the view window. Right click> Edit Compound Data, change the Calibration time and Injection time to the Start time. Set the Residual time to the start time plus 1 hour. Select change.

   Note: From Paravision 360 v3.6 the default reference time applied in the decay correction is the start of the acquisition, so this step is not necessary. Users who prefer the old methodology which is to have the dose calibration as the reference time can also do so.

6. Dynamic, no attenuation correction: P2: Main window, OSEM 0.5, Iteration Mode = auto, iterations = 1, Scatter correction with Dual energy Mode, Randoms correction, Partial Volume Correction, Point Spread Function Correction. Partitioning > Dynamic Reconstruction = 10X60; 4x300; Apply.

7. Dynamic, with attenuation correction: P3: Main window, OSEM 0.5, Iteration Mode = auto, iterations = 1, Scatter correction with Dual Energy Mode, Randoms correction, Partial Volume Correction, Point Spread Function Correction and Attenuation Correction (check VIBE P3 is selected). Partitioning>Dynamic Reconstruction = 10X60; 4x300; Apply.

8. Geometry registration: Images are then registered when loaded into PMOD.

9. Register to dynamic Coronal images P4. Right click P3 > Create Image Series > Image Registration (geometry based). A new window open, drag the MGE_2echo_cor into the source image series box and select execute. Right click>rename processing> add MGE in the name.

10. Registration (geometry based) VIBE sagittal images P5. Right click P3 > Create Image Series > Image Registration (geometry based). A new window open, drag the VIBE P2 into the source image series box and select execute. Right click>rename processing> add VIBE in the name.

    Note: From Paravision 360 v3.6 Denoising of the MR images. If required, the MR images and be reconstructed with denoising included. highlight the experiment and right click and select MRI Data Reconstruction. Select the Denoising tab and select suitable parameters,

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