Impact of Animal Handling on the Results of 18F-FDG PET Studies in Mice

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Abstract

Small-animal PET scanning with 18F-FDG is increasingly used in murine models of human diseases. However, the impact of dietary conditions, mode of anesthesia, and ambient temperature on the biodistribution of 18F-FDG in mice has not been systematically studied so far. The aim of this study was to determine how these factors affect assessment of tumor glucose use by 18F-FDG PET and to develop an imaging protocol that optimizes visualization of tumor xenografts. Methods: Groups of severe combined immunodeficient (SCID) mice were first imaged by microPET with free access to food, at room temperature (20°C), and no anesthesia during the uptake period (reference condition). Subsequently, the impact of (a) fasting for 8–12 h, (b) warming the animals with a heating pad (30°C), and (c) general anesthesia using isoflurane or ketamine/xylazine on 18F-FDG biodistribution was evaluated. Subcutaneously implanted human A431 epidermoid carcinoma and U251 glioblastoma cells served as tumor models. Results: Depending on the study conditions, 18F-FDG uptake by normal tissues varied 3-fold for skeletal muscle, 13-fold for brown adipose tissue and 15-fold for myocardium. Warming and fasting significantly reduced the intense 18F-FDG uptake by brown adipose tissue observed under the reference condition and markedly improved visualization of tumor xenografts. Although tumor 18F-FDG uptake was not above background activity under the reference condition, tumors demonstrated marked focal 18F-FDG uptake in warmed and fasted animals. Quantitatively, tumor 18F-FDG uptake increased 4-fold and tumor-to-organ ratios were increased up to 17-fold. Ketamine/xylazine anesthesia caused marked hyperglycemia and was not further evaluated. Isoflurane anesthesia only mildly increased blood glucose levels and had no significant effect on tumor 18F-FDG uptake. Isoflurane markedly reduced 18F-FDG uptake by brown adipose tissue and skeletal muscle but increased the activity concentration in liver, myocardium, and kidney. Conclusion: Animal handling has a dramatic effect on 18F-FDG biodistribution and significantly influences the results of microPET studies in tumor-bearing mice. To improve tumor visualization mice should be fasted and warmed before 18F-FDG injection and during the uptake period. Isoflurane appears well suited for anesthesia of tumor-bearing mice, whereas ketamine/xylazine should be used with caution, as it may induce marked hyperglycemia.

Keywords

18F-FDG, microPET, SCID mice, study conditions, brown adipose tissue
We recommend

Optimal experimental conditions for the detection of lung metastasis tumor using a small animal PET

Best Practices for Preclinical 18F-FDG PET Imaging
Olivia Kelada et al., J Nucl Med, 2018

Absolute Quantification of Regional Cerebral Glucose Utilization in Mice by 18F-FDG Small Animal PET Scanning and 2-14C-DG Autoradiography
Hiroshi Toyama et al., J Nucl Med, 2004

Effects of Anesthetic Agents and Fasting Duration on 18F-FDG Biodistribution and Insulin Levels in Tumor-Bearing Mice
Kyung-Han Lee, J Nucl Med, 2005

Enhancement of brown adipose tissue metabolism through adrenergic system activation quantifiable with 18F-FDG PET/CT in mice
M Reza Mirbolooki et al., J Nucl Med, 2012

Molecular Imaging of GLUT1 and GLUT5 in Breast Cancer: A Multitracer Positron Emission Tomography Imaging Study in Mice
Melinda Wuest et al., Mol Pharmacol, 2018

Positron emission tomography (PET) imaging of neuroblastoma and melanoma with 64Cu-SarAr immunoconjugates.

Coronary Adventitial and Perivascular Adipose Tissue Inflammation in Patients With Vasospastic Angina
PracticeUpdate, 2018

18F-FDG PET-CT in Detecting Cancer of Unknown Primary
PracticeUpdate, 2012

Loss of the Par-1b/MARK2 polarity kinase leads to increased metabolic rate, decreased adiposity, and insulin hypersensitivity in vivo.