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Anesthesia effects on [^{18}F]FDG biodistribution in mice using small animal PET

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1. Introduction

Experiment condition of animal handling impacts on the biodistribution of [18F]fluoro-2-deoxy-D-glucose ([^{18}F]FDG) in mouse study [1]. Toyama et al. [2] have evaluated the effects of anesthesia on [^{18}F]FDG uptake in the mouse brain and heart. Several studies have reported anesthetic effects on glucose and insulin level in mice [3,4,5]. However, no in vivo studies of anesthesia level have been reported using Positron emission tomography (PET) imaging in mice. The aim of this study was to evaluate the effect of anesthesia level and experimental condition on [^{18}F]FDG uptake in the mouse of small animal PET imaging.

2. Methods and Results

2.1 Animal preparation

The experimental conditions were 20 ± 2 h fasting and warming temperature at 30℃. Mouse body temperature was 35.8℃ after 30 min pre-warming. The heating pad was a plastic pad with water filed chamber. C57BL/6 (6 weeks old) mice were anesthetized using 2% isoflurane with oxygen for tail vein injection.

2.2 Normal mice Biodistribution

Female C57BL/6 (6 weeks old) mouse was injected with 20 μCi/0.1 mL of [^{18}F]FDG via the tail vein. To determine the impact of anesthesia during the uptake, five groups (n = 5) were studied as follows: no anesthesia, Ketamine 80 mg/kg and Xylazine 7 mg/kg, 0.5%, 1%, and 2% isoflurane. For biodistribution experiments, animals were sacrificed 1 h after radiotracer administration. Organs were excised, weighed and assayed for ^{18}F radioactivity in the 1480 WIZARD 3"automatic gamma counter. Figure. 1 shows the results of biodistribution for various anesthesia level in mice. 0.5% isoflurane anesthesia markedly decreased [^{18}F]FDG uptake by the heart.

2.3 Small animal PET imaging

Small animal PET image was started 60 min after ^{18}F-FDG (7.4 MBq in 0.1 mL) injection. We acquired a MicroPET R4 (Concorde Microsystems Inc., Knoxville, TN), which uses LSO crystals, 350 – 750 keV energy window and allows timing windows of 6 nsec [6]. The mouse was scanned for 20 min static image.

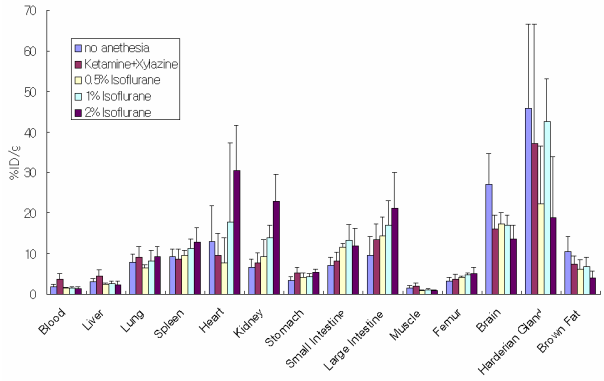

Figure 1. Biodistribution of [^{18}F]FDG in mice for various studied conditions. Experimental condition (no anesthesia, Ketamine/Xylazine, 0.5% isoflurane, 1% isoflurane, 2% isoflurane during uptake period) is shown as a comparison. Error bars show SD.

The heating pad is a carbon pad and mouse anesthetized by isoflurane, and temperature maintained at 30℃. The small animal PET data were reconstructed using ordered subsets expectation maximization (OSEM) algorithm with 4 iterations [7]. Figure. 2 shows the results of small animal PET imaging.

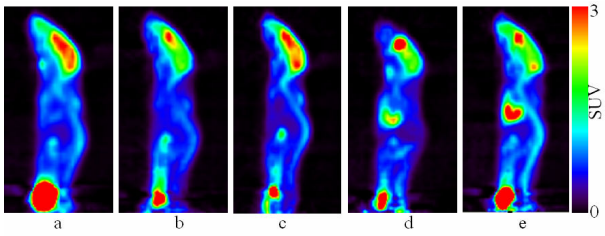

Figure 2. [^{18}F]FDG small animal PET images under various conditions in normal C57BL/6 mice. (a) No anesthesia, (b) Ketamine/Xylazine anesthesia, (c) 0.5% isoflurane anesthesia, (d) 1% isoflurane anesthesia, (e) 2% isoflurane anesthesia.

2.4 Quantitation of [^{18}F]FDG uptake

Glucose levels were measured after anesthesia for scanning. Average blood glucose concentration in normal mice was 92.25±19.16, 128.00±23.87, 83.50±21.75, 88.50±33.51, and 86.00±21.6 mg/dL in no anesthesia, Ketamine/Xylazine, 0.5%, 1%, and 2% Isoflurane, respectively. Ketamine/Xylazine group showed 1.5-fold higher blood glucose concentration than isoflurane used groups. Compared pattern of [^{18}F]FDG uptake and glucose standard uptake value

(SUV_G) of lung region between no anesthesia and anesthesia in normal mice. SUV_G is normalized for blood glucose level of 5.55 mmol/L (100 mg/dL) [8]. Lung to Background ratio (L/B) in SUV_G image was 2.71±0.75, 2.14±0.48, 3.03±0.63, 0.47±0.1, and 0.53±0.14 in no anesthesia, Ketamine/Xylazine, 0.5%, 1%, and 2% isoflurane, respectively. 0.5% isoflurane anesthesia group showed the highest L/B ratio.

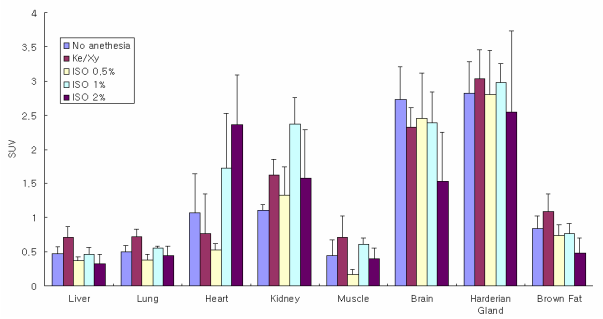

Figure 3. Biodistribution of [^{18}F]FDG in small animal PET images that were anesthetized during uptake period. Error bars show SD.

3. Conclusion

Animal studies with [^{18}F]FDG small animal PET should be considered fasting, warming, and isoflurane anesthesia level for reduction of background artifacts. This experimental condition improves the quantitative specific activity of the tracer. In tumor detection in lung region, ^{18}FDG image of 0.5% isoflurane anesthesia was better than that of Ketamine/Xylazine anesthesia during uptake period, because of high L/B ratio. This condition will be of most importance for small lesion detection of lung metastases tumor model.

REFERENCES

[1] B. J. Fueger, J. Czernin, I. Hildebrandt, C. Tran, B. S. Halpern, and, D. Stout D, et al, Impact of animal handling on the results of 18F-FDG PET studies in mice, J Nucl Med, Vol 47, pp999-1006, 2006.
[2] H. Toyama, M. Ichise, J. S. Liow, D. C. Mines, N. M. Seneca, K. J. Modell, and et al, Evaluation of anesthesia effects on [^{18}F]FDG uptake in mouse brain and heart using small animal PET, Nucl Med Biol, Vol 31, pp.251-256, 2004.
[3] T. Torizuka, A. C. Clavo, and R. L. Wahl, Effect of hyperglycemia on in vitro tumor uptake of tritiated FDG, thymidine, L-methionine and L-leucine, J Nucl Med, Vol 38, pp.382-386, 1997.
[4] K. J. Langen, U. Braun, Rota Kops E, H. Herzog, T. Kuwert, B. Nebeling, and et al. The influence of plasma glucose levels on fluorine-18-fluorodeoxyglucose uptake in bronchial carcinomas, J Nucl Med, Vol 34, pp.355-359, 1993.
[5] C. Gordon. Temperature Regulation in Laboratory Rodents, New York: NY; 1993.
[6] C. Knoess, S. Siegel, A. Smith, D. Newport, N. Richerzhagen, A. Winkeler, A. Jacobs, R. N. Goble, R. Graf, K. Wienhard, and W. D. Heiss, Performane evaluation of the MicroPET R4 PET scanner for rodents, Eur. J. Nucl. Med. Mol. Imaging, Vol 30(5), pp.737-747, 2003.
[7] H. M. Hudson and R. S. Larkin, Accelerated Image Reconstruction Using Ordered Subsets of Projection Data, IEEE Trans Med Imag, Vol. 13, pp.601-609, 1994.
[8] N. Paquet, A. Albert, J. Foidart, and R. Hustinx, Within-patient variability of (18)F-FDG: standardized uptake values in normal tissues, J Nucl Med, Vol 45, pp.784-788, 2004.