Visualizing the myocardial blood volume and cerebrovascular blood volume of rats using 18F-FDG labeled red blood cells and micro PET/CT

Shaowei Wang[1], Mikalai Budzevich[2], Mahmoud Abdalah[3], Kenneth L. Gage[4] and Jung W. Choi[4,5]

1.Department of Medical Engineering, University of South Florida, Tampa, FL USA; 2. Small Animal Imaging Laboratory (SAIL), H. Lee Moffitt Cancer Center & Research Institute ,Tampa, FL USA; 3. Image Response Assessment Team, H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL USA; 4. Department of Diagnostic Imaging, H. Lee Moffitt Cancer Center & Research Institute Tampa, FL USA; 5. Department of Cancer Physiology, H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL USA.

Background

We have recently shown that human red blood cells (RBCs) spontaneously incorporate amounts of the PET tracer 18F-FDG sufficient for non-invasive visualization of the total body vasculature of immunodeficient mice. Using an equivalent labeling protocol, we show here that rat RBCs can also be similarly labeled with FDG and used to visualize the myocardial and cerebrovascular blood volume of rats with microPET/CT. We further demonstrate that increases in the myocardial blood volume or cerebrovascular blood volume of rats can be detected on PET/CT after pharmacologic challenge with an appropriate vasodilator (regadenoson for myocardial imaging; acetazolamide for cerebrovascular imaging). Finally, we present preliminary data showing that FDG-labeled RBCs can be used to indirectly visualize the location of myocardial infarction in a rat after surgical ligation of the left coronary artery. These results suggest that FDG-labeled RBC PET imaging may be useful for visualizing the microvasculature of a target organ, as well as quantitating pathologic changes in the total volume of the organ microvasculature.

Methods

Fresh blood is collected from the rat saphenous vein and centrifuged 10 minutes at 1000g to separate the plasma and RBC pellet. The cell pellet is washed with 4 x volume of “1x EDTA” solution (140 mM NaCl，4 mM KCl，2.5 mM K_2EDTA dihydrate). After RBC washing, 100 µl 5x EDTA and 50 µl deionized water are added to 250 µl washed RBCs. 100 µl FDG (2 mCi) are then added to the RBCs. RBCs are then placed in a 37 °C incubator 30 minutes under gentle motion with a platform shaker. RBCs are then washed twice with 1xEDTA/5mM glucose solution. FDG-labeled RBCs are then injected into the rat through a tail vein catheter, and the rat is imaged in a Siemens Inveon microPET/CT platform. For myocardial blood volume imaging, the rat is first given regadenoson (6.5 µg in 100 µl 1x EDTA) prior to microPET/CT imaging to image the heart under pharmacologic myocardial “stress” conditions. After the first imaging session, pharmacologic myocardial stress reversal is achieved by administering aminophylline (13 mg in 200 µl deionized water), and the rat heart is imaged again. For rat cerebrovascular imaging, rats are imaged before and after administration of (35 mg in 200 µl 1x EDTA) of acetazolamide.

Results

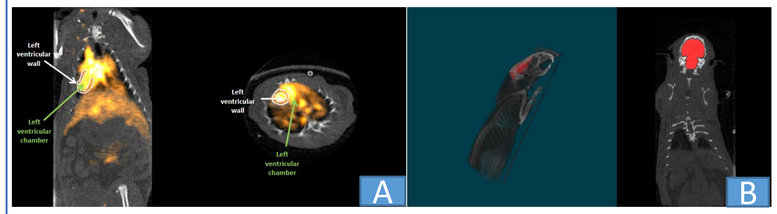


Figure 1. A: Fused FDG RBC PET/CT images of a rat after regadenoson injection. Coronal (left) and axial (right) segmentation of normal rat left ventricle myocardium. B: Fused sagittal 3D PET/CT rat brain image (left) and coronal brain segmentation (right).

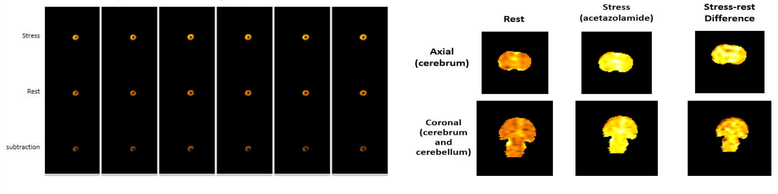
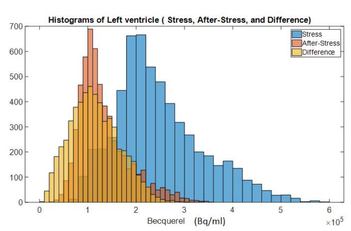
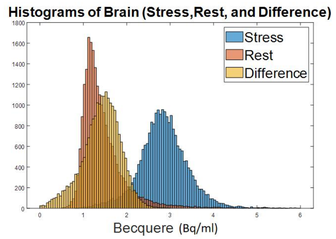


Figure 2. Left: Volume segmentation of rat left ventricular (LV) wall on FDG RBC PET images (short axis LV view) under “stress” (Regadenoson) and rest (aminophylline) conditions, with “stress - rest” (subtraction) imaging. Right: Axial and coronal FDG RBC PET images of the rat brain before (rest) and after (stress) acetazolamide administration, with “stress – rest” subtraction images.



	Heart Muscle Mean ('Bq/ml')
Stress	2.4722e+05
After-Stress	1.3220e+05
Difference	1.1502e+05



	Heart Muscle Mean ('Bq/ml')
Stress	2.850674
Rest	1.440164
Difference	1.418445

Figure 3. Histogram of FDG activity of myocardial (left ventricle) blood volume and cerebrovascular (brain) blood volume under stress (vasodilator) and rest conditions, with net increase in blood volume activity after subtraction of rest activity from stress activity (stress – rest difference).

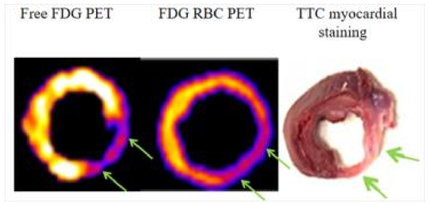


Figure 5. Area of decreased LV myocardial blood volume activity on FDG RBC PET (middle) correlates spatially with area of decreased myocardial metabolism on free FDG PET (left) as well as to the area of infarcted rat myocardium after TTC staining of the left ventricle (right) in a rat after left coronary artery ligation.

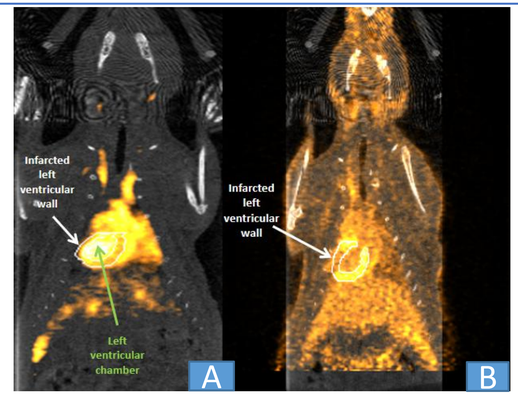


Figure 4. A: LV myocardial volume segmentation of FDG-labeled RBC PET/CT images from a rat after left coronary artery ligation. B: LV myocardial volume segmentation of FDG PET/CT images of the same rat after left coronary artery ligation.

Conclusions

We show that FDG-labeled RBCs can be used to image the microvasculature of the rat heart and brain with microPET/CT. In addition, we are able to detect increases in the myocardial blood volume (myocardial blood volume reserve) and cerebrovascular blood volume in rats after administration of the pharmacologic agents regadenoson and acetazolamide, respectively. This method may be useful for quantifying organ microvascular volume, as well as characterizing changes in the organ microvasculature in various pathologies, including coronary microvascular dysfunction.

Main References

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Disclosures

The research is under going, no specific disclosures.

Contact: Dr. Jung W. Choi, Moffitt Cancer Center

Email: jung.choi@moffitt.org