Noninvasive Image-Based Quantification of 18F-fluoromisonidazole (FMISO) Uptake using PET/MRI

Dragana Savic[1], Youngho Seo[1], Randall Hawkins[1], Soonmee Cha[1], Miguel Pampaloni[1], Sharmila Majumdar[1], and Ramon Barajas[1]
[1]*Radiology and Biomedical Imaging, University of California, San Francisco (UCSF), San Francisco, California, United States*

Purpose

Quantification of uptake in tissue of 18F-fluoromisonidazole (FMISO) currently requires invasive hemotologic sampling. This methodology conveys undue patient discomfort and handling of hazardous biological specimens. A newly introduced integrated PET/MRI modality provides an unprecedented spatial resolution at a high signal-to-noise (SNR) ratio due to the time-of-flight (TOF) PET imaging capability and a small PET detector ring diameter. Taking advantage of both improved spatial resolution and SNR, we developed a noninvasive imaging-based method for quantifying tissue radioactivity in patients administered with FMISO.

Approach

A resolution phantom with 9 different sized cylinders (ranging from 4.5 mm in diameter to 37.8 mm) containing a known activity concentration was scanned on an investigational hybrid simultaneous PET/MRI scanner (GE Healthcare, Waukesha, WI) using TOF-PET and T2-weighted (TE/TR, 3000/103 ms) MR sequences. Prior to scanning, three liquid samples from the phantom were withdrawn, and an average activity concentration was measured using a gamma counter (Wizard 1470, PerkinElmer, Waltham, MA). The calculated values from the PET scan and from the gamma counter were compared and the gamma counter efficiency was determined. For the *in vivo* quantification, we acquired two 40-minute PET/MRI data in patients with Gliomas (Oligoastrocymas), 90 minutes after the 259 MBq (7 mCi) FMISO administration. Attenuation and scatter corrections were applied to all PET reconstructions using the manufacturer provided algorithms. The patients were scanned head first with the manufacturers 8-channel brain coil. The MRI scan was acquired simultaneously with the PET scan. During the blood sampling the patient was not moved from the scan position, which was verified by not seeing any motion on the scans. Three different PET summed images were compared, 40 minutes summed (i.e., over 90-130 minutes) with TOF reconstruction, the second 20 minutes summed (i.e., over 110-130 minutes) with TOF reconstruction, and the second 20 minutes without TOF reconstruction. The last reconstruction was performed to simulate a PET/MRI scanner without TOF-PET imaging capability. T2-weighted images were used to draw regions of interest (ROI) about the resolution markers allowing for measure of activity concentration. Using the phantom data, six different partial volume correction (PVC) curves were determined using activity concentration values obtained from the different sized cylinders in the phantom to derive recovery coefficients. The patient PET data were corrected using PVC recovery coefficients derived from the phantom study. Both the maximum and the average activity concentrations in each ROI were investigated.
As an independent gold standard measurement, 5 ml whole blood venous samples were withdrawn from the patients, at 3 different time points with 10 min intervals following 90 minute uptake time, during PET/MR imaging of the brain. The average activity concentration from the blood samples was calculated by applying the gamma counter efficiency. All three blood samples were used when comparing to 40 min PET data, and only the third blood sample was used for the 20 min PET data. An ROI (3-4mm in diameter) about at the level of the proximal petrous bone segment of the internal carotid artery and jugular vein was located on the sagittal T2 image following the calculation of the average and maximum activity obtained from the 3 different fused PET/MRI reconstructions. The activity concentrations were corrected for the partial volume and the physical decay. An image based MRI blood-to-blood ratio (MB/B) was determined for all ROI's at the time of injection.

Results

The noninvasive imaging-based methodology demonstrated a reproducible quantification of the blood activity concentration that was not readily feasible using conventional lower-resolution PET/CT. **Table 1** shows the MB/B ratios for the carotid artery and the jugular vein ROI values and **Figure 1** shows the fused PET/MRI images. The average MB/B ratio is 1.16 for the carotid, when using the 40-minute TOF PET data. When using the 20-minute TOF PET data, the MB/B ratio is 0.93 for the carotid, showing that the correlation is similar for both scans. We have to note that that only the last blood sample at 30 min was used to compare to the 20 minute PET data.

MRI Blood-to-blood ratio (MB/B)	Patient 1: Max activity		Patient 2: Max Activity	
	Carotid	Jug. Vein	Carotid	Jug. Vein
MAC 40 min PET VPFX	1.03	1.07	1.27	1.29
MAC 20 min PET VPFX	0.59	0.71	1.07	1.14
MAC 20 min PET VPHD	2.22	2.05	3.27	3.23

Table 1. MRI Blood-to-blood ratio (MB/B) for the carotid arteries and the jugular veins. 40 min PET data was compared to all three blood samples (90-130 min) and the 20 min PET data was compared to the last blood sample (130min). The maximum activity in the ROI was used.

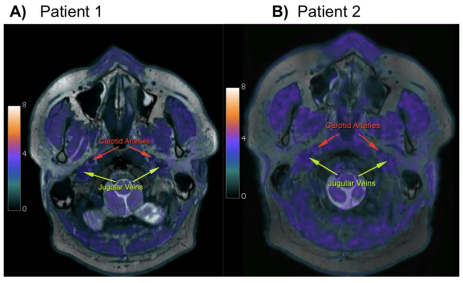

Figure 1. Axial view of fused PET/MRI brain scans of patient 1 (**A**) and patient 2 (**B**). PET 40 min MAC fused with Sagittal T2 weighted CUBE, TR 1800, TE 85.7, slice thickness 1.00mm. The carotid arteries (red arrows) and jugular veins (green arrows) are illustrated. PET values are scaled from SUV 0-8.

Discussion

We provide our initial experience with a noninvasive imaging-based method for quantifying FMISO tissue activity concentration using the image-derived blood concentration data. These preliminary results suggest that we can do the image-derived blood activity concentration calculation reproducibly, potentially avoiding invasive blood sample procedures. This quantification method only appears applicable, when the full capability of TOF-PET/MRI is used, which is a strong indication that the much improved spatial resolution and SNR are essential for the success of image-based blood activity quantification.

Conclusion

Our preliminary results show that a noninvasive quantification method for estimating the activity is feasible. Based on this method, we will also quantify the tumor-to-blood ratios in FMISO PET/MRI in patients with FMISO uptake in tumors.