A Study on the Optimal Image Acquisition Time of ^{18}F- Flutemetamol using List Mode

Chan-Ju Ryu[1,2,*]

[1]Department of Nuclear medicine, Bundang Cha Hospital

[2]Department of Radiological Science, Eulji University

Received: October 20, 2021. Revised: November 26, 2021. Accepted: November 30, 2021

ABSTRACT

With the development of Amyloid PET Tracer, the accuracy of Alzheimer's diagnosis can be improved through the identification of beta-amyloid neurites. However, the long image acquisition time of 20 minutes can be difficult for the patient. PET/CT scans are sensitive to patient movement and may partially affect test results. In this study, we studied the proper image acquisition time without affecting the quantitative evaluation of the image through the list mode acquisition method according to the time of the distribution of radioactive drugs in the body. The list mode includes information about time compared to the existing frame mode, and it is easy to analyze data because it can reconstruct images about the time that researchers want. The research method obtained a reconstructed image by time using a list mode of 5min frame/bed, 10min frame/bed, 15min frame/bed, and 20min frame/bed to compare the difference between signal-to-pons take ratio (SNR) and lesion-to-pons uptake ratio (LPR) and the difference in reading time to obtain an appropriate image. As a result of quantitative analysis, when measuring in list mode, SUVmean values decreased in 6 regions of interest as the image acquisition time increased, but showed the largest difference in 5 min/bed images, followed by 10 min/bed and 15 min/bed. As a result, the difference in SUVmean values decreased. Therefore, it was found that SUVmean values at 15 min/bed did not differ enough to not affect image evaluation. There was no difference in LPR values. As a result of the qualitative analysis, there was no change in the reading findings according to the PET image acquisition time and there was no significant difference in the qualitative analysis score of the image reconstruction according to time. As a result of the study, there is no significant difference between 15 min/bed and 20 min/bed images during the ^{18}F-flutemetamol PET/CT test, so it can be said that it is clinically useful to reduce the image acquisition time selectively using 15 min/bed via list mode depending on the patient's condition.

Keywords: Amyloid PET, Reconstruction, List Mode, Standardized Uptake Value

I. INTRODUCTION

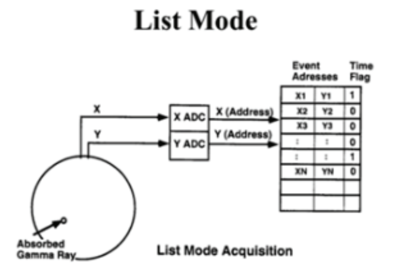
According to the Alzheimer's Association, it affects 13 % of people over the age of 65, and is the fifth most common cause of death among patients in this age group[1]. WHO predicts that by 2050, 114 million of the world's population will be expected[2]. Although the exact cause of Alzheimer's dementia is not known, many experts believe that the protein called amyloid, which is normally decomposed and discharged, is not decomposed but accumulates between nerve cells and interferes with normal brain function[3,4]. Originally, beta-amyloid in the brain could only be confirmed through post-mortem autopsy, but with the development of Amyloid PET Tracer, it has become possible to confirm it in living patients, and the accuracy of diagnosis can be improved by confirming the patient's beta-amyloid neurite[5]. The safety and effectiveness of

* Corresponding Author: Chan-Ju Ryu E-mail: ddrk18@naver.com Tel: +82-31-780-5682
Address : 59, Yatap-ro, Bundang-gu, Seongnam-si, Gyeonggi-do, Republic of Korea

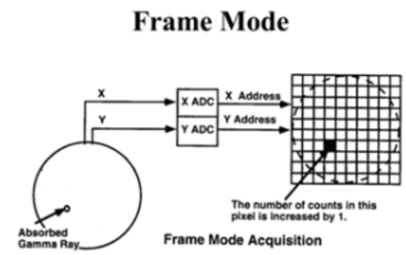
this test method has been proven through approvals from the U.S. Food and Drug Administration (FDA_October 2013), the European Medicines Agency (EMA_August 2014) and the Japan Pharmaceutical and Medical Devices Agency (PMDA_May 2015). In Korea, the product was approved by the Ministry of Food and Drug Safety in August 2015 and was evaluated for new medical technology by the Ministry of Health and Welfare in February 2016, and was marketed in March 2016[6]. ^{18}F-Flutemetamol ima -ges are visually read by comparing the activity of white matter and cortical gray matter. Pons become a reference for other regions, and if more than one region of five regions: frontal lobes, posterior cingulate and precuneus, lateral temporal lobes, parietal lobes, and striatum is positive, the corresponding image is classified as positive[7]. ^{18}F-flutemetamol PET/CT takes 20 minutes to film, can cause patient movement due to long image acquisition time, resulting in image quality degradation, delay in work due to re-shooting, and patient inconvenience.

The image acquisition method of PET(Positron Emission Tomography) can be divided into list mode and frame mode according to the method of recording events that occurred during PET scan as shown in Fig. 1[8]. List mode records all kinds of information (time and spatial position, energy of gamma rays, etc.) about all events (such as gamma ray detection, frame or bed start signals, trigger signals for gates, etc.) during image acquisition time. If all necessary information is recorded in the list mode data in the future, it can be converted into various types of frame mode data desired by the user[9].

Recently, the list mode acquisition method has been widely used to find out the distribution of radiopharmaceuticals in the body as changes with time[10]. Compared to the existing frame mode, the list mode includes information about time, so researchers can reconstruct images for a desired time separately, making it easier to analyze data.



(a) List Mode Method Image Acquisition Method



(b) Frame mode method image acquisition method

Fig. 1. Positron Emission Tomography (PET) Image Acquisition Method.

As for the reconstruction method of the list mode, in the previous study, the reconstruction method of the gate image, which was corrected for movement by synchronizing the respiratory cycle of the lungs, was used[11]. In addition, through a study that evaluated the usefulness of the list mode with a physical Jaszczak and IEC phantoms phantom[12], in this study, motion artifacts were eliminated through event-specific reconstruction by applying the patient's flutemetamol image due to a long recording time as a head motion correction method. By comparing and analyzing the difference in image quality and flutemetamol uptake ratio, we find an appropriate image acquisition time that does not affect the image result due to the movement of the patient, shortening the patient's examination time and improving the quality of medical care. It is expected that it will be useful in clinical practice.

II. MATERIAL AND METHODS

The subjects of this study were 165 people (76 males, 89 females, and 71.7 ± 4.7 years of average

age) who took this test from March 2016 to February 2021. The research equipment used in this study was Biograph mCT (SIEMENS Medical System, Germany) hardware equipment and MIM https://www.mimsoft ware.com, CEA, version 6.8.6) software equipment. The photographing conditions and image reconstruction factors using Biograph mCT (SIEMENS Medical System, Germany)are shown in Table 1.

Table 1. Sources Imaging Condition and Image Reconstruction Factor

CT		PET	
KV	120	Output image type	Corrected
Slice	3.0 mm	Recon method	TrueX+TOF (UltraHD-PET)
Increment	1.5 mm	Iterations	4
Pitch	0.8	Subsets	21
FOV	500 mm	Image size	256
Reconstruction algorithm	SAFIRE (Strength3)	Zoom	2.0
Reconstruction kernel	J30s medium smooth	Filter	Gaussian
EFF,mAs	CARE Dose 4D	FWHM	3.0 mm

The research method was conducted in quantitative and qualitative methods. By reconstructing the raw data of 165 people who have performed the test in list mode for 20 minutes, image acquired data for 5, 10, 15, and 20 minutes is derived. Based on the reconstructed data, in order to evaluate the overall amyloid uptake rate in the brain cortex according to the image acquisition time, ROIs were set for the entire part of the anterior cingulate gyrus, posterior cingulate gyrus, frontal lobe, parietal lobe, temporal lobe, precuneus and pons, The average standardized uptake value (SUVmean) for each area was measured for each image acquisition time (5 min/bed, 10 min/be d, 15 min/bed, and 20 min/bed).

Quantitative evaluation proceeds in two ways. First, the SUVmean values of 6 ROIs (Anterior cingulate gyrus, Posterior cingulate gyrus, Frontal lobe, Parietal lobe, Temporal lobe and Precuneus) measured by image acquisition time are measured, and the SUVmean values of 6 ROIs of the remaining data are compared based on the data acquired at 20min/bed. Second, the value obtained by dividing the SUVmean value of the six areas measured by the SUVmean of the pons used as the standard area for ^{18}F-flutemetamol analysis was defined as the lesion-to-pons uptake ratio(LPR), and this result was defined as calculated, and compared with the LPR values in the remaining data based on the obtained data for 20 min/bed[11].

$$SUV = \frac{\Upsilon}{(\alpha'/\omega)} \quad (1)$$

where γ is the radioactivity activity concentration [kBq/ml] measured by the PET scanner within a region of interest (ROI), α' is the decay-corrected amount of injected radiolabeled FDG [kBq], and ω is the weight of the patient [g], which is used a surrogate for a distribution volume of tracer[12].

$$LPR = \frac{ROI\ SUV_{mean}}{Pons\ SUV_{mean}} \quad (2)$$

For qualitative evaluation, the results of readings of a total of 165 study subjects were checked, and positive and non-amyloid-deposited and negative images with amyloid deposition were randomly selected. The nuclear medicine reading doctor confirmed whether the image quality evaluation and reading changed according to the image acquisition time.

III. RESULT

1. Quantitative Evaluation

The average of SUVmean values by image acquisition time for 6 regions of interest is shown in Table 2.

Table 2. Comparison of SUV Values of Regions of Interest according to Image Acquisition Time.

Area	5 min	10 min	15 min	20 min
1	0.79	0.80	0.80	0.80
2	1.13	1.11	1.09	1.03
3	1.01	1.00	0.98	0.96
4	1.39	1.36	1.34	1.30
5	1.29	1.27	1.25	1.22
6	1.26	1.24	1.22	1.18

As the image acquisition time increases, the SUVmean value of the region of interest decreases. Table 3 shows the differences in SUVmean values of 6 ROIs according to the image acquisition time based on the acquired data at 20 min/bed. As the image acquisition time becomes shorter, the difference in SUVmean values of the ROI from the reference data tends to increase, and the data acquired for 5 minutes showed an average 6.82 % lower SUVmean value for the region of interest than the data acquired for 20 minutes.

Table 3. Comparison of SUV Values of Regions of Interest according to Image Acquisition Time

Area	5 min	10 min	15 min
1. Anterior cingulate gyrus	-6.77	-4.84	-2.79
2. Frontal lobe	-6.14	-4.31	-2.44
3. Parietal lobe	-5.88	-4.70	-2.22
4. Posterior cingulate gyrus	-7.29	-4.70	-2.80
5. Precuneus	-6.25	-4.57	-2.50
6. Temporal lobe	-6.82	-4.45	-2.75
Average	-6.82	-4.60	-2.58

Secondly, Table. 4 show the result of the uptake ratio (lesion-to-pons uptake ratio, LPR) to the pons obtained by dividing the SUVmean value of 6 areas by the SUVmean of the pons used as the standard area for flutemetamol analysis. It appears that the LPR value of each region of interest does not change significantly depending on the image acquisition time. 20 min/bed The results of comparing the LPR values in the remaining data based on the acquired data are shown in Table 5.

Table 4. Comparison of SUV Values of Regions of Interest according to Image Acquisition Time

Area	5 min	10 min	15 min	20 min
1	0.79	0.80	0.80	0.80
2	1.13	1.11	1.09	1.03
3	1.01	1.00	0.98	0.96
4	1.39	1.36	1.34	1.30
5	1.29	1.27	1.25	1.22
6	1.26	1.24	1.22	1.18

Table 5. The Difference in LPR Value according to the Image Acquisition Time of the Region of Interest with Respect to the Reference Data

Area	5 min	10 min	15 min
1. Anterior cingulate gyrus	1.35	-0.19	0.11
2. Frontal lobe	1.78	0.23	0.34
3. Parietal lobe	2.14	-0.01	0.70
4. Posterior cingulate gyrus	1.09	0.06	0.16
5. Precuneus	1.47	0.70	0.25
6. Temporal lobe	1.19	-0.05	0.17
Average	1.50	0.12	0.29

From the reference data, the LPR value according to the image acquisition time was closest to the 10-minute data, followed by 15 minutes and then 5 minutes. The data acquired for 5 minutes showed that the LPR value of the region of interest was 1.5% higher on average than the data acquired for 20 minutes.

2. Qualitative Evaluation

We extracted 15 positive data with amyloid deposition and 10 negative data without amyloid deposition and performed qualitative evaluation on total 25 amyloid images. As a result, the 15-minute image showed little difference in image quality compared to the 20-minute image and was judged to be a significant image for reading. The quality of the 5-minute images and 10-minute images was significantly lowered, but it was not unreadable. In addition, there was no difference in the reading according to the image acquisition time, so there was no change in the reading findings according to the time.

IV. DISCUSSION

An image acquisition time of 20 minutes can be difficult for the patient. PET/CT scans are sensitive to patient movement and may partially affect test results. Therefore, in this study, the purpose of this study is to optimize the image quality from PET data acquired in list mode despite the patient's movement activity during the examination. When the image was reconstructed in the list mode, the SUVmean value was decreased in the 5 and 10 minutes images, but it did not affect the LPR value and the qualitative evaluation of the images. The best list method is the best time not to affect the SUV value, LPR value and image reading result from 15 min/bed, which can reduce the patient's image acquisition time by 5 minutes. When inspecting in list mode, reconstruction is possible according to various times, and if SNR measurement is performed at each time, more effective results will be obtained. In addition, it is thought that the retest rate will be reduced by reconstructing the image so that the patient's movement can have little impact on the reading, and furthermore, the radiation exposure caused by the retest will be reduced.

V. CONCLUSION

In this study, amyloid PET images using the list mode method were reconstructed and analyzed for each frame divided by time. In the quantitative evaluation, as the image acquisition time increased, SUVmean values decreased in 6 regions of interest, but showed the largest difference in 5 min/bed images, and the differences in SUVmean values decreased in the order of 10 min/bed and 15 min/bed. It was found that SUVmean values at 15 min/bed did not differ enough to not affect image evaluation. There was no difference in the part of the LPR value. In the qualitative evaluation, as a result of a blind test of two doctors over 5 years, there was no change in the reading findings according to the image acquisition time. It was confirmed that the image quality was lowered, but the image was not unreadable. Through the evaluation of the study, it is thought that accurate clinical results can be derived even after 15 minutes of imaging because the difference between the 15-minute imaging time image evaluation was small for 20 minutes of imaging time.

Reference

[1] Antoine Leuzy, Eduardo Rigon Zimmer, Kerstin Heurling, Pedro Rosa-Neto, Serge Gauthier, "Use of amyloid PET across the spectrum of Alzheimer's disease: clinical utility and associated ethical issues", Amyloid: The Journal of Protein Folding Disorders, Vol. 21, No. 3, pp. 143-148, 2014. http://dx.doi.org/10.3109/13506129.2014.926267

[2] K. B. Taek, "Evaluation of the Image Quality According to the Image Acquisition Time on the F-18 Flutemetamol PET/CT Image", Department of Radiology, Graduate School, Dongshin University, 2017.

[3] Y. T. Sik, "Temporal and Anatomical Distribution of 18F-flutemetamol Uptake in Canine Brain Using Positron Emission Tomography", Department of Veterinary Medicine, Graduate School, Chungbuk National University, 2017.

[4] M. K. Kim, H. I. Kim, J. H. Lee, S. H. Park, M. C. Song, "Status of quality control of medical Dose calibrator", The Korean Journal of nuclear medicine technology, Vol. 11, pp. 578-579, 2017.

[5] I. K. Hong, S. T. Chung, H. K. Kim, Y. B. Kim, Y. D. Son, Z. H. Cho, "Ultra-Fast Symmetry and SIMD-Based Projection-Backprojection (SSP) Algorithm for 3-D PET Image Reconstruction", IEEE transactions on medical imaging, Vol. 26, No. 6, pp. 789-803, 2007. https://doi.org/10.1109/tmi.2007.892644

[6] J. H. Kim, E. J. Lee ,S. S. Park, J. H. Heo, "A Case of Early Onset Alzheimer's Disease Diagnosed by 18F Flutemetamol PET Image", Dementia and Neurocognitive Disorders, Vol. 17, No. 4, pp. 174-4175, 2018. https://doi.org/10.12779/dnd.2018.17.4.174

[7] J. J. Lim, S. H. Yoon , J. P. Kim, "Evaluation of Image Quality Based on Time of Flight in PET/CT", The Korean Journal of Nuclear Medicine Technology, Vol. 16, No. 2, pp. 110-114, 2012.

[8] J. Y. Lee, E. K. Lee. K. W. Kim, H. W. Jeong, K. Y. Ryu, "Evaluation and Comparison of Contrast to Noise Ratio and Signal to Noise Ratio According to Change of Reconstruction on Breast PET/CT", Journal of radiological science and technology, Vol. 40, No. 1, pp. 79-85, 2017. http://dx.doi.org/10.17946/JRST.2017.40.1.12

[9] G. C. Hong, S. M. Park, I. S. Kwak , H. C. Lee, "The Optimization of Reconstruction Method Reducing Partial Volume Effect in PET/CT 3D Image Acquisition", The Korean Journal of Nuclear Medicine Technology, Vol. 14, No. 1, pp. 13-17, 2010.

[10] H. J. Choi, B. J. Kim, Mikiko. I, H. J. Lee, "Linearity Estimation of PET/CT Scanner in List Mode Acquisition", The Korean Journal of Nuclear Medicine Technology, Vol. 16, No. 1, pp. 86-90, 2012.

[11] Zheng. Zhang, Sean. Rose, Jinghan. Ye, Amy. E Perkins, Buxin. Chen, "Optimization-Based Image Reconstruction From Low-Count, List-Mode TOF -PET Data", lIEEE Trans Biomed Eng, Vol. 65, No. 4, pp. 936-946, 2018. https://doi.org/10.1109/TBME.2018.2802947.

[12] X. Jin, Chi. Liu, Richard E. Carson, "List-mode Reconstruction for the Biograph mCT with Physics Modeling and Event-by-Event Motion Correction", Physics In Medicine and Biology, Vol. 58, No. 16, pp. 5567-91, 2013. https://doi.org/10.1088/0031-9155/58/16/5567.

[13] Lehovich. A, "List-mode SPECT reconstruction using empirical likelihood", Department of Health Sciences Radiology, Graduate School, The University of Arizona, 2005.

[14] S. M. Park, S. Y. Kim, S. W. Choi, "The Evaluation of Dynamic Continuous Mode in Brain SPECT", The Korean Journal of Nuclear Medicine Technology, Vol. 21, No. 1, pp. 15-22, 2017.

[15] R. J. Walledge, R. Manavaki, M. Honer, A. J. Reader, "Inter-Frame Filtering for List-Mode EM Reconstruction in High-Resolution 4D PET", IEEE transactions on nuclear science, Vol. 51, No. 2, pp. 705-711, 2004. http://dx.doi.org/10.1109/TNS.2004.829783

[16] J. W. Yu, S. K. Woo, Y. J. Lee, K. M. Kim, J. S. Kim, "Estimation of Internal Motion for Quantitative Improvement of Lung Tumor in Small Animal", Korean Journal of Medical Physics, Vol. 22, No. 3, pp. 140-147, 2011.

[17] Y. H. Do, H. J. Lee, J. E. Kim, "Evaluation of Perfusion and Image Quality Changes by Reconstruction Methods in 13N-Ammonia Myocardial Perfusion PET/CT", The Korean Journal of Nuclear Medicine Technology, Vol. 18, No. 1, pp. 69-75, 2014.

[18] Y. K. Kang, Y. H. Kang, K. J. Kim, *The textbook Nuclear Medicine*, 2nd Ed., Chung-Ku Publishing Co., Korea, pp. 644-649, 2018.

LIST mode를 이용한 ^{18}F-Flutemetamol 의 최적 영상획득 시간에 관한 연구

류찬주[1,2,*]

[1]분당차병원 핵의학과
[2]을지대학교 방사선학과

요 약

핵의학은 방사성 동위원소 추적자를 인체에 투여하여 질병의 형태학적 정보와 생물학적 기능 정보를 얻고 평가한 Amyloid PET Tracer 개발로 베타아밀로이드 신경반 확인을 통해서 알츠하이머 진단의 정확도를 높일 수 있다. 그러나 20분이라는 긴 영상획득 시간은 환자에게 힘든 시간 일 수 있다. PET/CT 검사는 환자의 움직임에 민감하며, 검사 결과에도 일부분 영향을 미칠 수 있다. 이에 본 연구에서는 체내 방사성 의약품의 분포를 시간에 따른 list mode acquisition 방법을 통해 영상의 정량적 평가에 영향을 미치지 않으면서 적절한 영상획득 시간 연구하였다. list mode는 기존의 frame mode에 비해 시간에 대한 정보가 포함되어 연구자들이 원하는 시간에 대한 영상을 별도로 reconstruction 할 수 있어 data 분석에 용이하다. 연구 방법은 5 min frame/bed, 10 min frame/bed, 15 min frame/bed, 20 min frame/bed 로 리스트 모드를 이용하여 시간별 재구성 영상을 획득하여 SNR(signal to noise ratio) 과 LPR(lesion-to-pons uptake ratio)의 차이와 판독의 차이를 비교 분석하여 적정한 영상획득시간을 알아보고자 하였다. 정량적 분석 결과 list mode로 측정 시 정량적 평가 결과, 영상획득 시간이 증가함에 따라 관심 영역 6개에서 SUVmean 값은 감소하였으나 5 min/bed 영상에서 가장 많은 차이를 보였고 10 min/bed 그리고 15 min/bed 순으로 SUVmean 값의 차이가 감소하였다. 따라서 15 min/bed 에서의 SUVmean 값은 영상의 평가에 영향을 끼치지 않을 만큼의 차이가 없다는 결과값이 나왔다. LPR 값의 차이는 없었다. 정성적 분석 결과, PET 영상획득시간에 따른 판독 소견의 변화는 없었으며 시간에 따른 영상 재구성의 정성적 분석 점수의 유의한 차이가 없었다. 연구 결과 F-18 flutemetamol PET/CT 검사 시 15 min/bed 과 20 min/bed 영상이 유의한 차이가 없으므로 환자의 상태에 따라 LIST MODE를 통해 선택적으로 15 min/bed 을 사용하여 영상획득 시간을 줄이는 것이 임상적으로 유용하다고 할 수 있다.

중심단어: 아밀로이드 양전자 방출 단층 촬영, 영상 재구성, 리스트 모드, 표준화된 섭취값

연구자 정보 이력

	성명	소속	직위
(단독저자)	류찬주	차 의과학대학 분당차병원	방사선사
		을지대학교 대학원 방사선학과	대학원생