Measurement of CMRgl Using 18FDG by Quantitative Positron Autoradiography - Establishment of Simplified Standarization Procedure and Evaluation of Rate Constants

著者	Kameyama M., Kawashima K., Shirane R., Tsurumi Y., Suzuki J., Ishiwata K., Ido T.
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Kameyama M., Kawashima K.*, Shirane R., Tsurumi Y., Suzuki J., Ishiwata K.* and Ido T.*

Division of Neurosurgery, Institute of Brain Diseases, Tohoku University School of Medicine

Division of Radioisotope Research, Cyclotron and Radioisotope Center, Tohoku University*

We have recently reported the basic principle, procedure and application of multiple labeled autoradiographic technique using positron emitting radionuclide tracers.[2-4,9,10] However, there still remains problems before establishing the quantitative procedure of the positron autoradiography. In the present study, we have made further investigation of this newly developed technique, especially to evaluate the real CMRgl using ^{18}F-fluorodeoxyglucose (FDG) on the basis of simple standarization procedure and calculated constants derived from ^{18}FDG itself.

Materials and Method

1) Gelatin of 0.2 gm was dissolved into 0.8 ml of distilled water at 60°C. After adding various dose of ^{18}F solution, it was cooled at 4°C, then frozen in powdered dry ice. Frozen gelatin was cut 20 μm thickness in a cryostat (Histostat, American Optical). The sections were collected on the cover slips and dried at room temperature. Sections were then exposed to the X-ray film(KODAK NMC-1) for 6 hours in the spring loaded cassette. The residual gelatin was weighed and counted ^{18}F radioactivity. Six hours later, sections were removed from the X-ray film and ^{14}C autoradiographic standards (Amersham) were exposed to the same X-ray film for 7 days instead. Development of X-ray film was followed by the denstitometric measurement (Sakura PDA-15) of ^{18}F sections and ^{14}C standards.

2) Male Wistar rats were anesthetized with sodium pentobarbital and decapitated at 1, 3, 5, 10, 20 and 45 minutes following the administration of ^{18}FDG. Sequential arterial blood samples were taken during the study. Autoradiography was processed by 6 hours exposure to the X-ray film followed by the 7 days exposure of ^{14}C standards, and rate constant of ^{18}FDG was determined. In some rats, ^{18}FDG was administered for 45 minutes at the scheduled speed so that the arterial level of ^{18}F radioactivity became constant to calculate lumped constant of ^{18}FDG in the rats. The determination of CMRgl using the value of lumped constant and rate constants derived directly from ^{18}FDG was done.

Results

1) The relationship between the density and the radioactivity was found in both ^{14}C and ^{18}F (Fig. 1, 2). (Note, the radioactivity of ^{18}F was decay corrected to the time of the exposure to the X-ray film and also was corrected by counting efficiency of the gamma counter used in this experiment). Thus the theoretical linear relationship between ^{14}C and ^{18}F was calculated as shown in Fig. 3.

2) The value of lumped constant was 0.724 ± 0.120 and those of rate constants and CMRgl in the brain structures were summarized in Table 1.

Discussion

The multiple labeled autoradiographic technique using positron emitting radionuclide tracer has been proved useful for not only to demonstrate multiple physiological informations but also to evaluate basic properties of the new traces for positron emission computed tomography.[1-6,8-10] However, among the unsolved problems of this new technique, one of the important factor before establishing the qualifying the procedure is the standarization process of positron autoradiography.

There have been several trials for making the autoradiographic standard using the short half life radionuclide tracers.[5,6,8] But it has been inevitable to make the standards in each experiments due to the very short half lives of the radionuclides used. To simplify this complex and time consuming process, we have tried to simplify the standarization step of quantitative positron autoradiography by using the commercially available, permanent ^{14}C standards. The reproducible results of liner relationship between the ^{18}F radioactivity and the optical density under the same experimental condition – the same X-ray film, the same exposure time at the same temperature and the same automatic developing machine – indicate that it is not necessary to make the standards of short half life radionuclide in each experiments for quantifying the regional radioactivity on autoradiography. Instead, it suggests that the quantifiable positron autoradiography can be underwent by simply using the ^{14}C standards if the experiment was performed under the same scheduled condition.

There has been a report to measure CMRgl in the rat using ^{14}C-FDG[7], however, measurement of CMRgl using ^{18}FDG on the basis of lumped constant and rate constants derived from ^{18}FDG has not been achieved yet. The values obtained in anesthetized rats through this study seems to be good agreement to those previously reported[7], which again support the feasibility of our new standarization process.

The standarization procedure of positron autoradiography we tried in this study is simple and reliable, and also care must be taken to use the value of the constants derived from ^{14}CDG when performing the quantitative autoradiography using ^{18}FDG.

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Table 1. The value of rate constants and CMRgl in the anesthetized rats.

	k_1 (min^{-1})	k_2 (min^{-1})	k_3 (min^{-1})	CMRgl (mg/100g/min)
AUDITORY CORTEX	0.217±0.017	0.304±0.066	0.053±0.005	8.25±0.64
FRONTAL CORTEX	0.181±0.006	0.211±0.024	0.034±0.004	6.15±0.78
THALAMUS	0.165±0.019	0.203±0.090	0.042±0.012	7.09±0.69
CORPUS CALLOSUM	0.065±0.005	0.168±0.052	0.043±0.009	3.66±0.24
INTERNAL CAPSULE	0.056±0.007	0.175±0.026	0.046±0.006	3.22±0.18

mean±SE

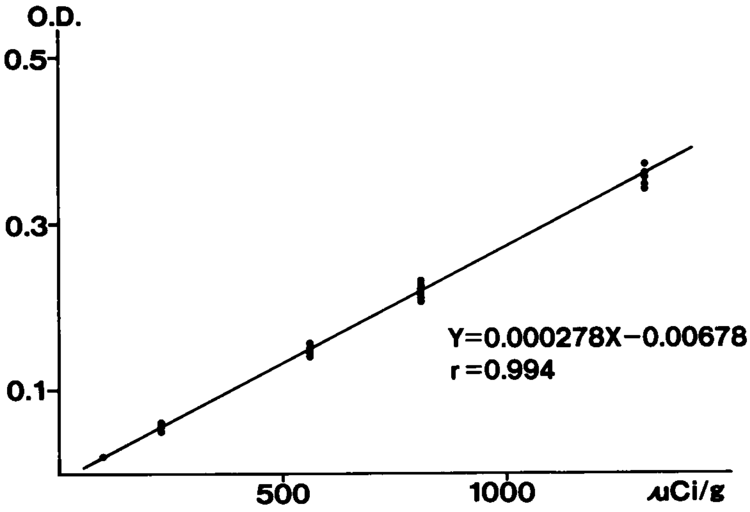

Fig. 1. ^{14}C radioactivity and optical density.

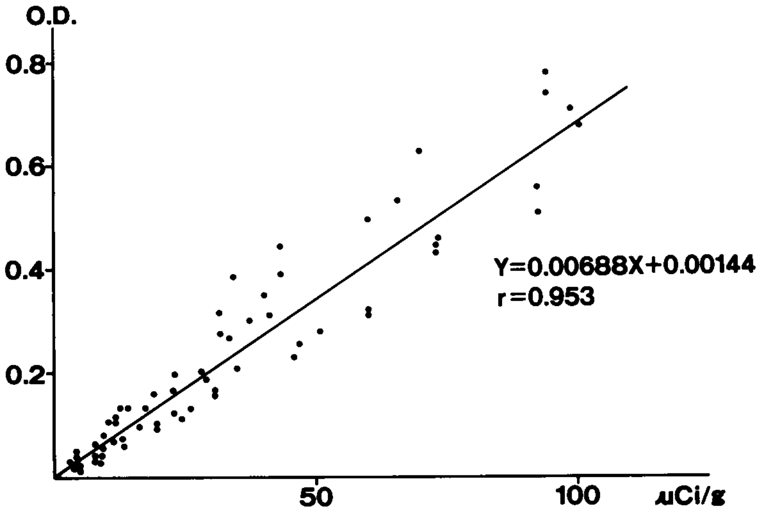

Fig. 2. ^{18}F radioactivity and optical density.

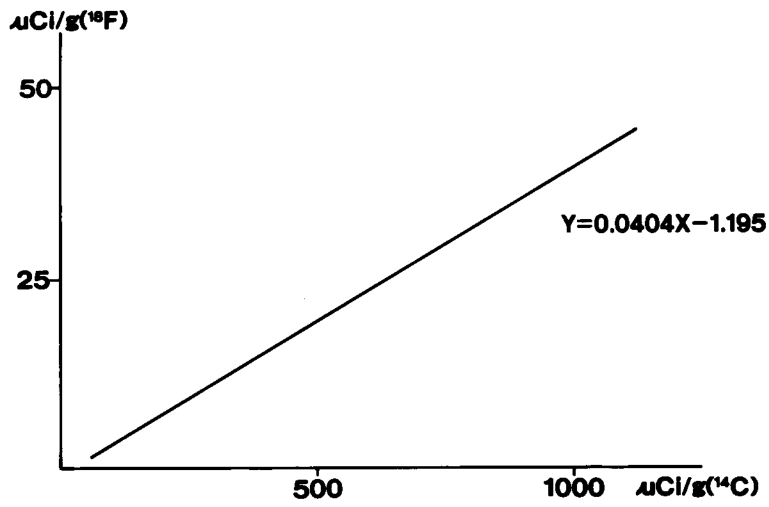

Fig. 3. The relationship between ^{14}C and ^{18}F on autoradiography.