1.3 Pharmaceutical and Others

Cell cycle dependency of ^{18}F-Choline uptake during proliferation of cultured human cancer cells

M. Shozushima, J. Yamamoto, Y. Hara*[1], K.Terasaki*[2], S. Goto*[3] and R. Iwata*[4]

Department of Dental Radiology, School of Dentistry, Iwate Medical University

19-1 Uchimaru, Morioka, 020-8505

*[1] Department of Oral Surgery, School of Dentistry, Iwate Medical University

19-1 Uchimaru, Morioka, 020-8505

*[2] Cyclotron Research Center, Iwate Medical University

19-1 Uchimaru, Morioka, 020-8505

*[3] Nishina Memorial Cyclotron Center, Takizawa Institute, Japan Radioisotope Association

348-58 Tomegamori, Takizawa, 020-0173 Japan

*[4] CYRIC Tohoku University

Aramaki, Aoba-ku, Sendai 980-8579, Japan

Abstract

Recently [^{18}F] labeled choline ([^{18}F] Choline) has been developed as a promising tracer for cancer detection; including ones found in the lung, prostate gland, head and neck regions. The experimental study demonstrated [^{18}F] Choline uptake was higher in faster-growing rather than in slower-growing tumors. However, the precise mechanism remains to be elucidated. In this study, the relationship between [^{18}F] Choline uptake and the cell cycle phase in cultured human cancer cells (HeLa S3), as well as how they compare to the conventional tracer [^{18}F] FDG with PET was assessed. Synchronization of HeLa S3 cells was accomplished via a double thymidine block. Flow cytometry (FCM) was used to determine the relative DNA contents of cells to check the degree of cell synchronization. The uptake of [^{18}F] Choline and [^{18}F] FDG was determined after cell cycle synchronization.FCM findings confirmed that the cells were well synchronized. [^{18}F] Choline uptake was 87% of the peak level in the early S-phase immediately after release, gradually increased, and peaked in the G2/M phase. Subsequently, [^{18}F] Choline uptake steeply declined over the late G2/M phase to 58% in the G1 phase. The results suggest that the uptake of [^{18}F] Choline is cell cycle dependent, is associated with the proliferative activity of the tumor seen during PET imaging.

Preparation and quality control of [^{18}F]NaF for clinical application

S. Goto[1], K. Terasaki[2], R. Iwata[3] and K.Sera[2]

[1]Nishina Memorial Cyclotron Center, Japan Radioisotope Association
348-58 Tomegamori, Takizawa, Iwate 020-0173, Japan

[2]Cyclotron Research Center, Iwate Medical University
348-58 Tomegamori, Takizawa, Iwate 020-0173, Japan

[3]CYRIC, Tohoku University
Aramaki, Aoba-ku, Sendai, Miyagi 980-8578, Japan

Abstract

[^{18}F]NaF is used for skeletal imaging. While some ^{99m}Tc-labeled pharmaceuticals such as [^{99m}Tc]methylene diphosphonate also have high affinity for bones and widely used, [^{18}F]NaF is considered to be more preferable agent in some viewpoints. One benefit of using [^{18}F]NaF is rapid blood clearance which serves shorter study time for patient convenience. [^{18}F]NaF is a simple compound and easily prepared only by eluting $^{18}F^-$ trapped on an anion exchange column (QMA) with normal saline or $NaHCO_3$ solution through a 0.20 μm membrane filter. However, [^{18}F]NaF injection produced by this way is subject to the quality of ^{18}O enriched water that is irradiated to produce ^{18}F, and the product is likely accompanied by some impurities such as vanadium-48 (^{48}V), a radionuclide with half-life of 15.97 days derived from irradiation of titanium target chamber. To use [^{18}F]NaF for clinical purpose, it is important to assure the quality. In this paper, content of impurities in samples taken at some points of [^{18}F]NaF preparation is analyzed by using PIXE method and pure-Ge semiconductor detector to find optimum conditions (ion form of QMA, kind of eluent and its volume) for preparing [^{18}F]NaF. Contamination is shown least in [^{18}F]NaF eluted with 2 mL of 0.4% $NaHCO_3$ solution. This suggests that inorganic nuclides such as ^{48}V are oxidized in aqueous solution and held trapped on QMA when $^{18}F^-$ is eluted with diluted $NaHCO_3$.

Automated [^{18}F]flumazenil synthesis in the F-100 FDG synthesizer

K. Terasaki*[1], Y. Ishikawa*[2], M. Shozushima*[3], S. Goto*[4] and R. Iwata*[2]

*[1]Cyclotron Research Center, Iwate Medical University
348-58 Tomegamori, Takizawa 020-0173, Japan

*[2]CYRIC, Tohoku University
Aramaki, Aoba-ku, Sendai 980-8578, Japan

*[3]Department of Dental Radiology, School of Dentistry, Iwate Medical University
19-1 Uchimaru, Morioka, 020-8505 Japan

*[4]Nishina Memorial Cyclotron Center, Japan Radioisotope Association
348-58 Tomegamori, Takizawa 020-0173, Japan

Abstract

[^{18}F]flumazenil ([^{18}F]FMZ), fluorine-18 labelled radiotracer, is that it possesses longer half-life (110 min) than carbon-11 and allows the examination of more patients per tracer production and the possibility of longer acquisition protocols. We performed the radiosynthesis of [^{18}F]FMZ by modifying the commercial FDG synthesizer module (F-100, Sumitomo Heavy Industries, Ltd.). [^{18}F]FMZ was synthesized by nucleophlic labelling of a solution of nitromazenil, nitro-precursor, in 0.5–1 mL of DMF using K^{18}F/Kryptofix 2.2.2 complex avoiding a performed azeotropic drying procedure. After semi-preparative HPLC purification, the [^{18}F]FMZ was obtained in 15–20% radiochemical yields (decay not corrected), with more than 95% radiochemical purity.

Control of accuracy of PET system

Toshiaki Sasaki[*1], Kuniaki Ogasawara[*4], Masakazu Kobayashi[*4], Yasunori Suga[*4], Kouhei Chida[*4], Satoru Hatakeyama[*2], Yshihiro Saito[*2], Shoko Goto[*2], Kazunori Terasaki[*1], Koichiro Sera[*1], Keizo Ishii[*3] and Akira Ogawa[*4]

[*1]Cyclotron Research Center, Iwate Medical University
348-58 Tomegamori, Takizawa, Iwate 020-0173, Japan

[*2]Nishina Memorial Cyclotron Center, Japan Radioisotope Association
348-58 Tomegamori, Takizawa, Iwate 020-0173, Japan

[*3]Department of Quantum Science and Energy Engineering, Tohoku University
6-6-01-02 Aoba, Aramaki Aobaku, Sendai, Miyagi 980-8579, Japan

[*4]Department of Neurosurgery, Iwate Medical University
19-1 Uchimaru, Morioka 020-8505, Japan

Abstract

In order to improve reliability of the quantitative values given by recent 3D-PET, we have started the studies according to the guidance consisting of five items. They are; 1. acquisition of the basic data by means of existing 2D-PET, 2. fundamental development of the method of quantification for 3D-PET, 3. designing of the phantoms for quality and performance of 3D-PET, 4. investigation of the actual statuses of the methods of PET-scan and diagnosis in other facilities, 5. improvement of accuracy and precision of the quantitative values given by 3D-PET.

The number of PET institutes has been increasing recently. Most of all PET cameras are 3D-PET or 3D-PET/CT. 3D-PET camera had increasing not only resolution and sensitivity but also scatter. Then we are afraid that increasing of scatter may cause decrease of PET quantitative.

In this study, we have experimented basis on the guideline for the performance evaluation of PET. But this guideline is not good for the 3D-PET cameras. Then we revised the guideline both sequencing and standard measurement. Usually we experiment performed resolution test at first, scatter fraction is second, and sensitivity is third. But sensitivity test needs about 5hours. It will be completely nothing the FDG by the time we are going to try other kind of PET performance tests. We in turn examined the PET performance test 1.spatial resolution, 2.scatter fraction, 3.partial volume effects, 4.scatter and absorption of accuracy correct, 5.uniformity, 6.sensitivity. Almost PET performance test of guideline are 5% of the scatter coincidence by true coincidence. We changed 10-20-% from 5% of guideline. Because we need to finish all PET performance tests within one or 2 days.

Result spatial resolution was approximately 6.02 mm full with half maximum in plane and 5.96 mm FWHM axially. Scatter fraction was about 51%. Sensitivity was 3914.7cps/(KBq/ml). Accuracy scatter correction, teflon 3.5%, air 27.3%, water 15.4%. Uniformity, -0.869%, round type of recovery coefficient, 38mm=1.0, 27mm=0.79 , 21mm=0.61, 16mm=0.43, 13mm=0.38, 10mm=0.17. Cylinder type of recovery coefficient, 38mm=1.0, 27mm=0.84, 21mm=0.73, 16mm=0.61, 13mm=0.61, 10mm=0.45.

The time for the PET performance test decreased 5hours from about a week after the change of the guideline. If we use this guideline changed method, we could experimented the PET performance more often. Then we will learn how often the PET performance test by year. We will enable to compare quantitative value of the PET between other PET facilities. But also we need to accurate PET performance tests basis on the guideline at once. We applied method is most validate to compare the PET performance. We are going to follow this method about one year.