A STEADY PRODUCTION OF [^{18}F]FDG WITH KIRAMS-13 CYCLOTRON AT KIRAMS

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Abstract

KIRAMS has designed and manufactured the [^{18}F]FDG production module in parallel with the development of KIRAMS-13 cyclotron. KIRAMS completed the development of both KIRAMS-13 cyclotron and [^{18}F]FDG production module and started a routine production of [^{18}F]FDG. The yield of [^{18}F]FDG produced is 51±2% in average at EOS, decay uncorrected. The operation system was developed with LabView (National Instrument) for the user interface system. A tetrabutyl ammoniumhydroxide (TBA) was used as a phase transfer catalyst and hydrochloric acid was selected for hydrolysis of triflate. The total time elapsed for the completion was 24±1 min. The quality of [^{18}F]FDG including radiochemical purity, radionuclidic purity, acidity, residual solvent, osmolality and endotoxin was evaluated after production. The examined contents for quality control of [^{18}F]FDG were found to be suitable for clinical application.

INTRODUCTION

2-[^{18}F]fluoro-2-deoxy-D-glucose ([^{18}F]FDG) is a widely used radiopharmaceutical for positron emission tomography (PET).[1,2] The main advantage of PET is early diagnosis in patients with cancer. [^{18}F]FDG can be produced by two types of [^{18}F]fluorination. Nucleophilic substitution method using [^{18}F]fluoride is preferred in [^{18}F]FDG production instead of electrophilic substitution method using [^{18}F-^{19}F]fluorine gas due to getting [^{18}F]FDG having high specific activity.[3] Although many [^{18}F]FDG modules equipped with fantastic disposable materials (cartridges, reagents and etc) are commercially available, commercialized [^{18}F]FDG module is usually hard to manipulate the program and modify the sequences when some changes are necessary such as reaction temperature or evaporation temperature or step time.

Recently, installation of cyclotron and PET-scanner are booming in Korea as well as [^{18}F]FDG production module. As a part of Regional Cyclotron Installation Project in Korea, we optimized our [^{18}F]FDG production module which will be installed at regional cyclotron centers. The features of our [^{18}F]FDG production module are easy operation and preparation as well as reproducible high yield. In addition, the operation program developed is easy to customize for application of other F-18 labelled radiopharmaceuticals such as *O*-(2-[^{18}F]fluoroethyl)-L-tyrosine (L-[^{18}F]FET) by hitting a few keystrokes.

METHODS AND RESULTS

The details will be discussed in this section

Main Frame

The prototype [^{18}F]FDG module was put together on an aluminum profile base which is a convenient frame and easy to assemble and dismantle during development. We have designed the frame chassis with 3-dimensional designing tool. We put up a large rear door to achieve an easy access to internal parts and maintenance. Main frame was anodized to prevent and reduce the oxidation and scratch during preparation

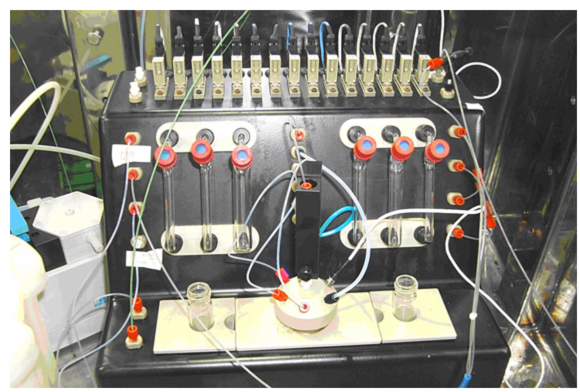

Figure 1: [^{18}F]FDG production module installed in hot cell, KIRAMS.

Fittings and glassware

PEEK polymer was used as a fitting material which holds on the glass ware and reaction vial. We designed and machined the material. PEEK is known as an inert material to a variety of chemicals including acid and base. The glassware has a glass net layer to prevent unwanted inflow of particle into the reaction vessel. PEEK fittings were designed for fingers tighten. Pressure of reaction vessel can affect the [^{18}F]FDG production yield during evaporation, [^{18}F]fluorination and hydrolysis steps. Kulite XT-123C-190 diaphragm type pressure transducer was directly installed on the reaction vessel head to monitor an accurate pressure during process.

Control Program

Programmable Logic Controller (PLC) was used for the previous version of module with touch pad display panel. We have developed on a computer based new operation program with LabView (National Instrument, USA) to get an easy variable settings and convenient customization. Temperature is controlled by means of electric on/off system and air cooling unit. This method showed small over heat during temperature control compared to PID control in PLC. The data is automatically acquired during process and exported as a text file (*.txt) with time frame after running in auto run mode.

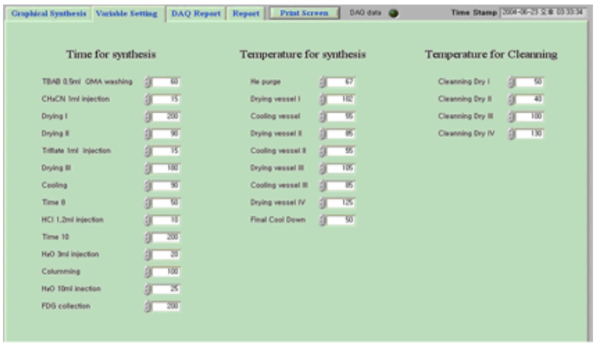

Figure 2: Main view of variable setting panel. Time and temperature can be changed.

Each tab represents as follows.

In the graphical synthesis tab, all information (elapsed time, step time, pressure, radio activity and temperature) are displayed in real time.

In the variable setting tab, time and temperature can be easily modified, that allows flexible application of development of other F-18 labelled radiopharmaceuticals.

In the DAQ report tab, reaction vessel pressure, elapsed time, reaction vessel temperature and radioactivity are displayed on each designated row.

Communication between control computer and [^{18}F]FDG production module is connected with I/O card and data communication cable.

[^{18}F]FDG production yield

F-18 was produced with KIRAMS-13 cyclotron by irradiation of $H_2{}^{18}O$ at Korea Institute of Radiological and Medical Sciences (KIRAMS).

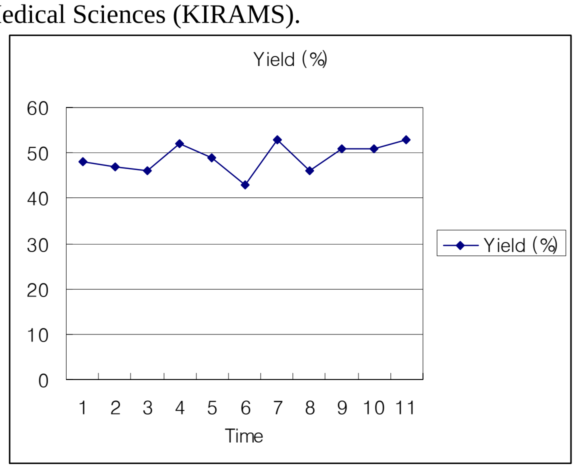

Figure 3: [^{18}F]FDG production yield during test period with KIRAMS [^{18}F]FDG module.

The yield was from 44% to 53% during test period and maintained 51±2% in routine production, decay uncorrected. [^{18}F]FDG production yield with our prototype module was from 38% to 45%.

[^{18}F]FDG Quality Control

The [^{18}F]FDG quality was determined by conventional methods

Table 1. Quality control data of [^{18}F]FDG

QC item	Value	Remarks
Radio-TLC (R_f)	0.45	OK
Radiochemical purity (%)	99	OK
MCA analysis	511.65	OK
Residual solvent (Acetonitrile, mg)	0.035	OK
Residual solvent (Ethanol, mg)	0.445	OK
Residual solvent (Acetone, mg)	0.487	OK
pH	5.22	OK
LAL test	-	OK
Asepsis test	pass	OK
Isotonicity (mOsm)	279	OK

The QC data are listed in table 1. All contents were satisfied with the standard value and proved to be suitable for clinical use.

CONCLUSION

In conclusion, KIRAMS [^{18}F]FDG production module has been designed, manufactured and evaluated. The quality of [^{18}F]FDG was proven to be suitable and safe for clinical use. KIRAMS [^{18}F]FDG module has shown high production yield with reproducibility and has been used for routine production with KIRAMS-13 cyclotron.

REFERENCES

[1] Shung, K. K.; Smith, M. B.; Tsui, B. M. W. Principles of Medical Imaging, 1992, Academic Press Inc.
[2] Ter-Pogossian M. M.; Phelps M. E.; Hoffman E. J. and Mullania A. Radiology, 114, 89, 1975.
[3] Stoecklin, G. and Pike, V. W. Radiopharmaceuticals for positron Emission Tomography, 1993, Kluwer Academic Publishers.