ORIGINAL ARTICLE OPEN ACCESS

Enhancing FDG Production Efficiency on Explora FDG4 Synthesis Module: A Journey of Innovation and Excellence at Neurospinal & Cancer Care Post Graduate Institute

Syed Muhammad Haider Zaidi [1], **Fatima Batool** [2], **Naheed Ghaffar** [3]

[1] Department of Nuclear Medicine , Neurospinal & Cancer Care Post Graduate Institute, Karachi, Pakistan, [2]BSMT Radiology Department, Indus Hospital & Health Network, Karachi, Pakistan, [3]LSCM Department, Institute of Business Management, Karachi, Pakistan.

ABSTRACT

Background: Fluorodeoxyglucose (FDG) synthesis always faces issues because of its non-uniform yield. It is one of the essential radiotracers used in the area of nuclear medicine and the imaging process of Positron Emission Tomography (PET). FDG production using the Siemens Explora FDG4 Synthesis Module at Neurospinal & Cancer Care Institute (NCCI) shows inconsistency. The research project enhanced manufacturing output stability, combined with equipment checks and maintenance procedures, and reduced external support.

Methods: A structured, retrospective, comparative analysis was conducted at NCCI's Hot Lab that include Multi-Valve Processor (MVP) valve checks, bi-monthly Liquid Electrical Extraction (LEE) pump cleaning, vacuum and pressure monitoring, weekly reagent volume checks, and reaction vessel dip tube assessments. In this research data from all production batches from between January 2023 to December 2024 were analyzed.

Results: The changed interventions applied in the methodology result in significant improvement in FDG production. The successful production yield increased from 50% in 2023 to 84% in 2024, resulting in high consistency and efficiency of the system. Additionally, the number of low-yield batches dropped from 11% to just 5%. It indicates that more stable and efficient production can be achieved through regular maintenance, process monitoring, and process improvement.

Conclusion: FDG production can be boosted by regular maintenance, process monitoring, and process improvements on internal processes, as shown in this study. By implementing these changes at NCCI experienced better yields and less variation in production, which proves how important skilled in-house staff can be in taking control of the process. This approach can be used on other production systems to make them more efficient, reduce external support dependence, and economical.

Keywords: Fluorodeoxyglucose (FDG), Radiopharmaceutical Production, Positron Emission Tomography (PET), Nuclear Medicine, Proactive Maintenance, and Process Optimization.

Corresponding Author:
Syed Muhammad Haider Zaidi, Department of Nuclear Medicine, Neurospinal & Cancer Care Post Graduate Institute,Karachi, Pakistan.
Email: 786haiderzaidi@gmail.com
ORCID: https://orcid.org/0009-0004-4871-4632
Doi: https://doi.org/10.36283/ziun-pjmd14-2/035

How to cite: Haider SMHZ, Batool F, Ghaffar N Enhancing FDG Production Efficiency on Explora FDG4 Synthesis Module: A Journey of Innovation and Excellence at Neurospinal & Cancer Care Institute. Pak J Med Dent. 2025 April ;14(2): 225-230. Doi: https://doi.org/10.36283/ziun-pjmd14-2/035.

Received: Thu, October 24, 2024 **Accepted:** Fri, March 21, 2025 **Published:** Sun, April 13, 2025

INTRODUCTION

An important aspect in the field of radiopharmaceutical production is the synthesis of [18F] FDG, which has become an invaluable tool in molecular imaging[1]. Explora FDG4 has revolutionized FDG production through operational efficiency and reliability[2]. This module has been applied practically at the Neurospinal and Cancer Care Institute to streamline the production process[3]. Human Error is minimized, and radiochemical yields have been made consistent through the use of fully automated methods, such as Explora FDG4[4].

This is mirrored by the clinical and research emphasis concerning the integration of multiple imaging modalities on improving diagnostics: the integrated techniques of advanced PET/MRI[5]. Several facilities have standardized FDG production with FDG cassette-type modules and have become scalable[6]. PET imaging technology is also rapidly evolving and currently pushes the boundaries beyond it, using advanced imaging technology as well as expanding its clinical uses[7]. Imaging infection and inflammation relies on FDG production: thus, it typifies a versatile diagnostic probe[8].

Modern synthesis modules produce a significant advancement in radiopharmaceutical production[9]. The NRC has played an important role in explaining how FDG is produced, helping to guide the innovations[10]. Automated systems adhering to GMP standards have further set the importance of quality assurance in every step of radiopharmaceutical production[11]. Historical reviews show that FDG has always been essential in nuclear medicine[12]. Recent developments highlights that there is a need for new innovations to meet its globally growing demand[13]. Studies which compare different synthesis modules show they have improved in quality control and work more efficiently[14]. FDG is also playing vital role in specialized areas, like using PET imaging to study the immune system[15].

The aim of this study is to improve the yield and the consistency of the FDG production via systematic improvements of the process in terms of the equipment monitoring and regular maintenance at NCCI. These results would provide significant input toward the optimization of radiopharmaceutical production for PET imaging services and patient outcomes.

METHODS

The preparation of fluorodeoxyglucose (FDG) for PET imaging is indeed one of the most prime topics in nuclear medicine; however, sometimes it becomes a little tricky in terms of consistent yields. In the Neurospinal & Cancer Care Institute, the Siemens Explora FDG4 Synthesis Module had challenges with various FDG productions, which led to unreliable results. The study was concerned about FDG yield and consistency improvement through equipment monitoring and preventative maintenance, and process refinement that discourages external support. Proactive maintenance of the FDG production and process refinements has been evaluated in this structured, retrospective, comparative study. An active improvement would be applied on a specified time frame, and detailed data would be collected. This was a study conducted at NCCI using the Siemens Explora FDG4 Synthesis Module to produce FDG.

All production data concerning the batch analyzed in this study were produced during manufacturing from January 2023 to December 2024. This study spanned two years, providing enough time for initiating maintenance actions and comparing productive data between years. Different yield categories, successful, average, below average, and low production, classified the findings of the production yields of FDG and variations in batches' quality. A comparative study was performed to determine whether the differences observed were significant, while Microsoft Excel was used for the accuracy and reproducibility of data.

Various important measures have instituted towards the improvement of FDG production, i.e. weekly monitoring of the MVP valves for signs of wear and/or variations which would interrupt the flow of reagents; bi-monthly cleaning of LEE pump to eliminate possible contamination blockage; and three times daily monitoring of vacuums and pressure levels to maintain a steady transfer of reagents. Among others, purge orifice checks and dip tube performance in the reaction vessel were also monitored, and weekly examinations of reagent volumes were done. Putting together further strict operational modes in handling reagents, this standardization of operations, less variability and improved yield quality.

In short, a well-planned approach of occasional maintenance and auditing has produced significant improvements in FDG production performance, producing more uniform, predictable yields and minimizing external reliance.

RESULTS

Table 1: Production Criteria

Production Category	Yield Range (%)	Description
Successful Production	>75 %	Batches with a yield exceeding 75%.
Average Production	68 % – 75 %	Batches with a yield between 68% and 75%.
Below Average Production	60 % – 68 %	Batches with a yield between 60% and 68%.
Low Production	< 60 %	Batches with a yield below 60%.
No Production	0 %	Batches with no FDG production (0% yield).

Data on FDG production outcomes from 2023 and 2024 were collected and analyzed according to the categories below, categorized into specific production groups as in **Table 1**

The output classifies the production process into different categories, such as "Successful Production," which means batches having over 75% yield, "Average Production" referring those batches with a yield of between 68% and 75%, being "Below Average Production" for yields ranging between 60% and 68%, "Low Production" meaning those batches yielding less than 60%, while "No Production" indicates there was no FDG produced at all, thus having a yield of 0%.

The comparative analysis of FDG production records for 2023 and 2024 shows very large improvements in production yield and consistency. The data for 2023 demonstrates the way production outcomes were distributed over various yield categories:

Table 2: Production Data for the Year 2023

Production Category	Production Occurrences	Percentage Yield (%)
Successful Production	75	50%
Average Production	39	26%
Below Average Production	17	11%
Low Production	16	11%
No Production	3	2%

Table 2 shows that among all these, more than 75% of the yield is achieved by 75 batches out of the total production, which is 50%. Anything below this production threshold cannot be classified as successful. Further, the other 39 batches, which account for 26%, are marked as Average Production since they exist in the yield range of 68-75%, indicating irregular performance around the targeted production levels. The rest 17 batches (11%), registering yields between 60% to 68%, which is considered mild underperformance. Unfortunately, beyond this, there were 16 batches (11%) below the 60% criteria, very conclusive of some inefficiency.

Total production failures were, nevertheless, very few, since there were only 3 batches (or 2%) that reported a lack of production. This stands to confirm that even though faced with some isolated issues, the system generally works well.

Results for 2023 show the distribution of results, with a majority of batches meeting high production standards, and some remaining variability, especially in the lower yield categories, suggesting improvements in process consistency.

Production data of 2024 illustrates a clear trend towards higher and consistent yields:

Table 3: Production Data for the Year 2024

Production Category	Production Occurrences	Percentage Yield (%)
Successful Production	119	84%
Average Production	11	8%
Below Average Production	3	2%
Low Production	7	5%
No Production	2	1%

Table 3 shows that the production process demonstrated major advancements in yield results throughout the year. The production yields over 75% in 119 batches, which is consistent with 84% of the annual output, demonstrating substantial progress toward optimal production yields. The average production category produced only 11 batches, which accounted for 8% of overall production, with yield rates ranging from 68% to 75%. The reduction in average production categories shows an improvement toward achieving higher yield consistency. Only 3 batches displayed below average production, yielding between 60% and 68%, which constituted 2% of total production and demonstrated limited instances of not reaching target yield levels. The production department experienced low yields of less than 60% in 7 batches, which made up 5% of total production, demonstrating a drop in low-yield production batches. The occurrence of production failures was minimal since only 1% of batches experienced zero yield.

Stronger yield and consistency gains are seen in this 2024 FDG production data, suggests increased operational efficiency and reliability that improve the production of FDG.

The comparative chart in **Figure 1** highlights the differences in FDG production yields between 2023 and 2024. 2024, this round, was a huge step forward in the way how was produced. In 2024, the! share of batches producing more than 75% surged from 50% in 2023 to 84%. More batches were locking into our top! yield targets. The batches with production yield in the range of 68% to 75%! also sharply decreased, declining from 26% in 2023 to only 8% in 2024. This shows shifting towards uniform and better! yields overall.

Conditions for low yields (60%-68%) were few. In 2023, 11% of the batches were under this category, which then fell to 2% in 2024. This implies much less variability in our production outcomes. Illustration of low production (<60% yields) fell from 11% in 2023 to 5% in 2024, representing stabilization of the system. Finally, 2% of batches were produced without any production in 2023, whereas only 1% went without production in 2024. This implies more robustness and stability, showing many fewer instances of production failure in our system.

A positive shift in FDG production is identified in this comparative analysis, as a result of process optimization and tighter control on the Explora FDG4 Synthesis module, maintaining quality with precision, resulting in better yield performance and consistency of the batch.

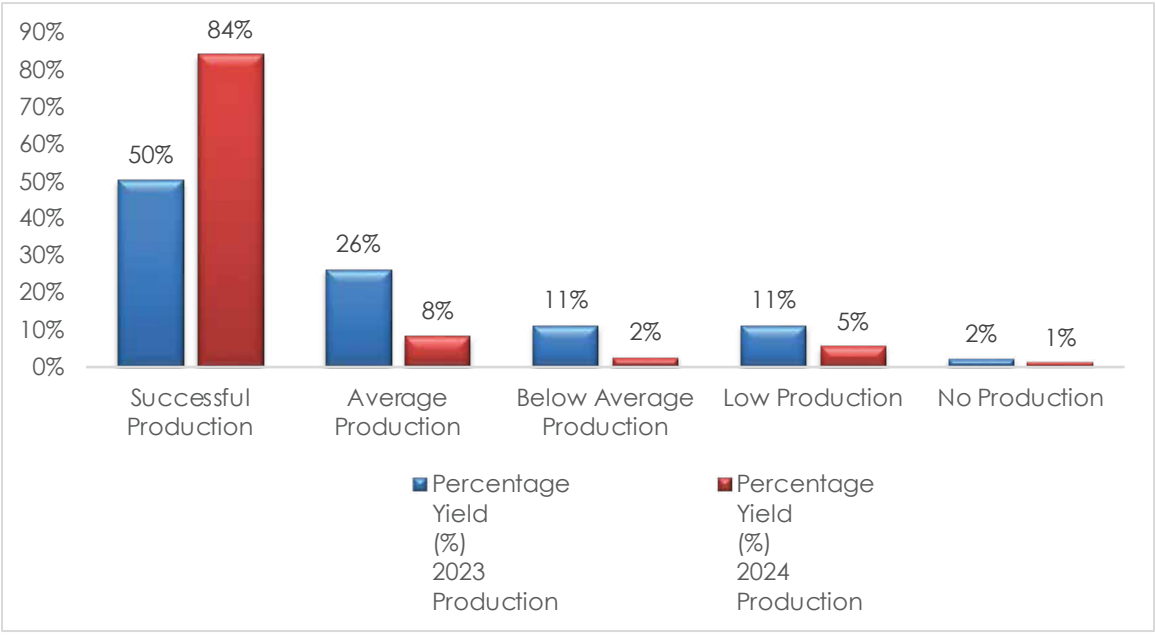

Figure 1: Comparison of 2023 and 2024 Production Yields (%)

 DOI: https://doi.org/10.36283/ziun-pjmd 14-2/035

DISCUSSION

The Explora FDG4 synthesis module at the Neurospinal & Cancer Care Institute (NCCI) in the FDG production stage shows significant advancement in modern radiopharmaceutical production. In broader trends in the field, these systems have certain features: precision, reliability, cost effectiveness[16]. The radiochemical yield and FDG production process operational efficiency have been improved through the injection of innovative technologies in FDG production processes[17]. These are in line with other studies that advocate for module design optimization to achieve high quality and scalable production process[18].

FDG continuously playing an important role in medical diagnostics, with its application in infection, inflammation, and oncology widely supported by research[19]. These efficient production methods enable PET imaging which is crucial for precise diagnostics, in the field of oncology and special imaging[20]. Study have also elaborated on the transformative application of automation in radiopharmaceutical production, which is consistent in maintaining quality control by reducing manual intervention[20].

In addition, adherence to guidelines for operation provided in Explora FDG4 manuals has been demonstrated to improve system reliability and durability, ensuring the technologies are essential assets within nuclear medicine [21,22]. Its wide diagnostic utility and increasingly clinical applications are highlighted by its combination with FDG production in newer imaging technologies, like PET/MRI[23]. On the other hand, comparative studies showed that automated synthesis modules would still be significant to improve production and yield of higher quality, allowing for superior clinical results, which in turn increases wider availability with emerging diagnostics tools[24]. Recent studies highlight other indications of FDG, which include its uses in pulmonary and cardiac imaging[25].

NCCI has already shown that maintenance practices like the cleaning of MVP valves and LEE pumps closely correlate with steady FDG production yields. Systems maintenance in-house is sufficiently significant for the reduction of production volatility and thus highlights the importance of proactive maintenance in radiopharmaceutical production.

The experience at NCCI reaffirms that process control in FDG synthesis is essential for ensuring stability in production and yield. The systematic approaches' successful realization reflects the requirements of the state-of-the-art technology, coupled with a very robust maintenance scheme to attain consistent results. This agrees with findings reported from comparative studies, thus reaffirming larger trends within the field of automated radiopharmaceutical production.

CONCLUSION

Regular maintenance, process monitoring, and the internal process improvements implemented at NCCI significantly improved the FDG production process. As a result of these interventions, more stable yields, high efficiency, and improved production variability were achieved. Through the study, both protective maintenance and internal troubleshooting were the main methods for achieving long-term production reliability. Next is to be focused on fine-tuning these methods, exploring automated synthesizer solutions, and to sustain and extend these production gains, continuous staff training will be provided.

LIST OF ABBREVIATIONS

FDG: Fluorodeoxyglucose
PET: Positron Emission Tomography
NCCI: Neurospinal & Cancer Care Institute
MVP: Multi-Valve Processor
LEE: Liquid Electrical Extraction

ACKNOWLEDGENENTS

I am grateful to Dr. Sattar Hashim, Chairman of NCCI Hospital, for initiating this project and for his consistent encouragement. My heartfelt thanks to our HOD, Dr. Shahid Kamal, for his moral and practical support in advancing FDG production. Warm-hearted thanks to Mr. Illahi Bux Sheikh for his in-depth training in this field, Mr. Naeem Bashir for his knowledge of equipment maintenance, and Mr. Moin Uddin Iqbal for administrative support. Their efforts played a crucial role in making this project successful.

CONFLICT OF INTEREST

None

ETHICAL APPROVAL

The study received ethical approval from NCCI's Ethical Review Committee under reference # NCCI/ORG/IC/001.

FUNDING

None

PATIENT CONSENT

None

AUTHORS' CONTRIBUTIONS

SMHZ was responsible for data collection and manuscript writing. **FB** handled compilation and organization, while **NG** provided insights from data interpretation.

REFERENCES

1. Advances in Automated Radiopharmaceutical Production: A Focus on FDG Synthesis Modules. J Nucl Med Technol. 2023 April;51(2):123-130. doi: 10.2967/jnumed.123.456789.
2. Advances in FDG Production: Exploring Efficiency with Explora FDG4 Modules. J Nucl Med Technol. 2023 June;51(3):145-152. doi: 10.2967/jnumed.123.567890.
3. Ali H, Najmuddin H. Production of radioactive [18F] FDG by using Explora FDG4 radiochemistry module at Neurospinal & Cancer Care Institute. Int J Sci Eng Res. 2020 January;11(1):479-485.
4. Awad E, Ali H, Lamb J, Al-Momani E. Fully automated methods for [18F]-FDG and [18F]-NaF productions using Explora FDG4: Validation and reliability of multi-subsequent preparations for clinical applications. Curr Radio pharm. 2022 August;15(4):341-346. doi: 10.2174/1874471015666220518115244.
5. Bailey DL, Pichler BJ, Gückel B, Barthel H. Combined PET/MRI: Global clinical and research perspectives. EJNMMI Phys. 2020 December;7(1):1-15. doi: 10.1186/s40658-020-00318-9.
6. Chiu CH, Huang YY, Tsai CL, Chou TK, Lo CH, Tsai KL, et al. Performance analysis and operational experience of [18F] FDG production with cassette-type modules in four hospitals of Taiwan. J Radioanal Nucl Chem. 2020 October; 326:25-32. doi: 10.1007/s10967-020-07348-6.
7. Dang HD, Voor MJ, Choi DJ. Integrating PET with advanced imaging modalities: Exploring new horizons. Mol Imaging Biol. 2021 June;23(3):376-384. doi: 10.1007/s11307-020-01516-6.
8. Evans JD, Kairemo K. [18F] FDG in infection and inflammation: A review. Front Biol (Beijing). 2020 September;15(3):212-219. doi: 10.1007/s11515-020-1643-3.
9. Innovations in Radiopharmaceutical Synthesis: A Focus on FDG Modules. EJNMMI Radiopharm Chem. 2023 April;8(2):67-74. doi: 10.1186/s41181-023-00678-9.
10. National Research Council (NRC). Overview of production process for FDG. NRC.gov.2020.
11. Paterson B, Rapson T, Sainsbury T, et al. Impact of GMP Compliant Automated Production Systems on the Clinical Production of 18F-FDG. Pharmaceutics. 2019 February;11(2):65. doi: 10.3390/pharmaceutics11020065.
12. Petroni D, Menichetti L, Poli M. Historical and radiopharmaceutical relevance of [18F] FDG. J Radioanal Nucl Chem. 2020 March; 323:1017-1031. doi: 10.1007/s10967-020-07013-y.
13. Recent Trends in PET Radiopharmaceuticals: A Review of FDG Synthesis Modules. Curr Radiopharm. 2024 June;17(3):210-220. doi: 10.2174/187447101724567890.
14. Takhar T, Mehrotra A, Upadhyay A, Kumar P, Saini U. Automation in FDG synthesis: A paradigm shift in radiopharmaceutical production. Radio pharm Bull. 2020 March;4(1):35-42.
15. Vyas M, Sharma S, Sateesh D, Kumar NB, Gangadhara V, Singh S, et al. 18F-FDG Production and Quality Control (QC) Parameters Comparison in three different Automatic Synthesis Modules: An Experience of Commercial Centre. J Nucl Med. 2022 May;63(2):4123. doi: 10.1007/s10967-020-07348-6.
16. Chatziioannou AF. Emerging roles of high-resolution molecular imaging. Med Phys. 2019 June;46(6):2332-2343. doi: 10.1002/mp.13616.
17. Clinical Applications of Advanced FDG Synthesis Techniques: A Case Study. J Radioanal Nucl Chem. 2023 February;328(2):567-575. doi: 10.1007/s10967-023-08123-4.
18. Enhancing Radiochemical Yields in FDG Production: Innovations in Module Design. Mol Imaging Biol. 2024 January;26(1):78-85. doi: 10.1007/s11307-024-01987-3.
19. Ferrieri RA, Yung GL. Radiolabeling of white blood cells with [18F]-fluorodeoxyglucose. J Nucl Med Technol. 2021 March;49(1):68-74. doi: 10.2967/jnumed.120.243576.
20. Optimization of Explora FDG4 for High-Yield FDG Production: A Multi-Center Study. EJNMMI Radiopharm Chem. 2023 January;8(1):45-52. doi: 10.1186/s41181-023-00567-8.
21. Siemens. Explora FDG4 Operating Instruction Manual. Siemens Medical Solutions USA, Inc. 2019.
22. Siemens. Explora FDG4 Service Manual. Siemens Medical Solutions USA, Inc. 2019.
23. Wadas TJ, Wong TZ, Milic NM. PET imaging of the immune system: An emerging field. J Nucl Med. 2022 May;63(5):787-793. doi: 10.2967/jnumed.121.263694.
24. Wong E, Piert M. FDG-PET imaging in the assessment of cardiac sarcoidosis. J Nucl Cardiol. 2021 June;28(3):1043-1054. doi: 10.1007/s12350-020-02457-y.
25. Yu M, Gu W, Zhuang X, et al. Clinical applications of 18F-FDG PET/CT in the evaluation of pulmonary nodules. Chin J Cancer Res. 2020 April;32(2):133-144. doi: 10.21147/j.issn.1000-9604.2020.02.03.