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Implementation of the CLIO Automated Dispensing System for [^{18}F] FDG: Enhancing Safety and Operational Efficiency at NINMAS

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ABSTRACT

The [^{18}F] 2-fluoro-2-deoxyglucose, [^{18}F] FDG is a commonly used PET radiopharmaceutical for imaging in cardiology, neurology, and oncology. Using an 18/9 MeV IBA cyclotron, [^{18}F] FDG is produced at the National Institute of Nuclear Medicine and Allied Sciences (NINMAS) and distributed to all PET-CT facilities in Dhaka. Manual dispensing of [^{18}F] FDG, involving repeated handling of high activity vials, was carried out for several batches before the CLIO (Volumetric dispensing system manufactured by COMECER) automated dispensing system was introduced at our institute to enhance efficiency, accuracy, and radiation safety. This study aimed toward evaluating the effectiveness of the CLIO automated dispensing system in [^{18}F] FDG production at NINMAS, with a particular emphasis on workflow quality, operational efficiency, and radiation safety in comparison to manual dispensing. The ^{18}O(p,n)^{18}F nuclear reaction was used to produce [^{18}F] Fluoride, which was synthesized to [^{18}F] FDG using an automated synthesis module (Synthera®). The manual approach involved measuring activity in a Dose Calibrator, diluting it to the necessary concentration, and then using syringes to dispense it into individual vials. In the automated process, CLIO used robotic handling to dispense pre calculated volumes in a shielded hot cell. The exposed radiations were recorded at approximately 30 cm, 1 m, and 2 m away from the dispensing site. TLD badges and pocket dosimeters were used to track individual doses. For both processes, operational metrics such as staffing, documentation, preparation time, dose repeatability, and delivery compliance were noted. The CLIO system reduced average radiation exposure by 80–97% across all measured distances, with the largest reduction at ~30 cm (45.0 ± 2.9 µSv/h to 9.0 ± 0.6 µSv/h). Pocket dosimeter readings decreased by 66.7% (30 µSv/day to 10 µSv/day), while TLD whole-body doses remained same (<0.05 µSv/day) in both workflows. Dose preparation time per vial decreased by 50% (2.0 ± 0.5 min to 1.0 ± 0.2 min), and staff requirements per cycle fell from three to two. Dose reproducibility improved from ±6.0% to ±1.5%, and on-time delivery compliance increased from ~82% to ~97%. Documentation and labelling errors were eliminated through digital batch logs and automated barcoding. These findings support the wider use of automated dispensing systems by demonstrating a decrease in radiation exposure for employees and an increase in operational efficiency in regular radiopharmaceutical production. The significant reductions in exposure, improved dose precision, and streamlined workflow support broader adoption of automated dispensing systems in PET radiopharmaceutical production facilities.

1. Introduction

Positron Emission Tomography and Computed Tomography (PET-CT), is a widely used diagnostic imaging technique to detect malignancy [1]. [^{18}F] 2-fluoro-2-deoxy glucose ([^{18}F] FDG), a glucose analog, is a frequently used PET tracer [2-3]. In the diagnosis of a variety of cancers, including as lung, lymphoma, colorectal, breast, and head and neck cancers, PET-CT has emerged as a gold standard for tumor staging, restaging, evaluating therapy response, and detecting recurrences [4]. [^{18}F] FDG

PET-CT is being used growingly in cardiology, neurology, and inflammatory imaging outside of cancer [5]. To ensure quality, safety, and effective distribution, automated synthesis and dispensing system advancements are critical [6]. As PET tracers like [^{18}F] FDG has a short physical half-life it requires precise timing in synthesis, quality control, dispensing, and delivery to guarantee optimal activity at the time of patient injection. The image quality may be interrupted for any kind of delay in dispensing and transportation [7]. Accurate dispensing of the radiopharmaceuticals is crucial for ensuring diagnostic accuracy and optimizing cost effectiveness. But in manual dispensing staffs are more likely to radiation exposure and risk of contamination through repeated handling of radioactive materials. Reducing manual manipulation through automation and shielding is necessary to cling to the ALARA (As Low as Reasonably Achievable) principle [8-9]. Thus, assessing the effectiveness of the CLIO automated dispensing system in [^{18}F] FDG production at NINMAS was the particular objective of the current study.

In facilities supplying radiopharmaceuticals to multiple PET-CT centers, automated dispensing is prime requirement to improve compliance as it includes batch recording, barcode scanning, and error reduction features. Automated dispensing smooths centralised production, speeds up turnaround times, and allows for scalable, reliable distribution over a large geographic area [10]. The National Institute of Nuclear Medicine and Allied Sciences (NINMAS), under umbrella of the Bangladesh Atomic Energy Commission (BAEC), owns a state-of-the-art 18/9 MeV IBA Cyclone® cyclotron, which serves as the government site for routine production of [^{18}F] FDG in Bangladesh. The Cyclotron facility at NINMAS fulfil the national demand for PET-CT imaging by producing clinical-grade [^{18}F] FDG maintaining Good Radiopharmacy Practice (GRP). The whole process of production and distribution is supported by a strong quality control (QC) system, which includes radionuclidic purity testing, pH verification, radiochemical purity by TLC, endotoxin testing, and filter, all performed in compliance with Pharmacopoeia and IAEA guidelines [11,12,13]. The facility has now implemented the CLIO automatic dispensing system, which greatly enhances dose accuracy, traceability, and worker safety after seeing the need for updated and safer processes.

Prior to automation, [^{18}F] FDG dispensing at our facility was conducted manually within lead-shielded hot cells. This method was efficient for small-scale manufacturing, but it required trained radiopharmacists to manually prepare, draw, and distribute to individual vials while adhering to strict radiation safety regulations [14]. Occupational exposure to dangerous ionizing radiation is one of the main problems associated with manual [^{18}F] FDG dispensing. Even with the use of protective lead barriers, radiopharmacy staff are at serious risk from radiation exposure, particularly during the dispensing period. Studies have shown that hand exposure can approach regulatory limits when multiple manual doses are prepared daily [15]. Manual dispensing is normally operator dependent, which introduces variability in dose volume accuracy, labelling, sterility assurance, and documentation. Errors in handling, incorrect volume calibration, or mislabelling of syringes can result in underdosing, overdosing. In radiopharmacy, manual dispensing limits the scalability of FDG distribution for a nationwide network, strains staff, and decreases operational efficiency [16]. Due to numerous human touch points, glovebox handling mistakes, and the absence of automated batch records, it further raises the risk of contamination and makes GMP compliance more difficult. As national demand for [^{18}F] FDG grows, the need to maintain high levels of standardization and reproducibility becomes paramount. Automated dispensing systems like CLIO address these issues by enabling precise volumetric control, ensuring that each dispensed dose meets exact clinical requirements [16]. Automation with the CLIO system reduces occupational radiation exposure by minimizing manual handling of high-activity doses, aligning with ALARA principles, and keeping staff at a safe distance through its shielded and closed design [14].

It enables rapid, precise multi-dose dispensing of vials, boosting workflow efficiency in high-throughput facilities like NINMAS and freeing personnel for tasks such as quality control and logistics. Its sterile, closed architecture lowers microbial contamination and human error risks, ensuring compliance with Good Radiopharmacy Practice (GRP) and pharmacopoeial sterility standards for patient safety [17]. Integrated digital batch recording, barcode labeling, and data archiving enhance traceability, documentation accuracy, and regulatory compliance under GMP while supporting audits and retrospective analyses [18-19].

2. Methods and Materials

This study's [^{18}F] FDG was synthesized at Cyclotron Division of the National Institute of Nuclear Medicine and Allied Sciences (NINMAS) using an 18/9 MeV medical cyclotron of IBA Cyclone®. With the capability to accelerate protons up to 18 MeV and deuterons up to 9 MeV, this dual beam cyclotron makes it able to produce a wide range of positron emitting radio-isotopes. The ^{18}O(p,n)^{18}F nuclear reaction was utilized to create ^{18}F by bombarding ^{18}O enriched water ($\geq$ 97%) in a niobium target chamber. 2-Fluro-2-Deoxy Glucose (^{18}F-FDG) was synthesized by using an automated synthesis module (Synthera®), installed inside the lead shielded hot cell. A lead-shielded cabinet was used at NINMAS to manually dispense [^{18}F] FDG doses prior to the installation of the CLIO automatic dispensing equipment. Trained persons carried out the whole procedure in a radiation-controlled environment. Following synthesis, [^{18}F] FDG was put into a glass vial that was shielded by a lead barrier. In the manual dispensing, the total activity of the produced [^{18}F] FDG was first measured in a calibrated dose calibrator (ISOMED 2010 Dose Calibrator Dresden, Germany) immediately. The volume was then diluted with sterile saline to obtain the desired concentration in mCi/mL. Based on this data, the volume required for each PET-CT facility is calculated manually. Using syringes, individual volumes were taken from this mother vial and dispensed into separate secondary vials according to the clinical requirements of various PET-CT facilities.

Fig. 1.: Manually Dispensing Unit at NINMAS.

Every dispensed vial was carefully labelled with the dispensed time and activity. At a distance of approximately 30 cm, 1 m, and 2 m from the dispensing site, a calibrated survey meter (Automess 6150 AD 5/H S/N 161475), was utilized to identify the absorbed radiation levels during dispensing of doses in vials. Staff exposure was monitored using a combination of whole-body TLD badge worn on the chest and pocket dosimeter (Polimaster PM1610) for real-time dose monitoring. The CLIO automated dispensing device, placed inside the lead shielded hot cell, received the bulk-produced activity straight from the synthesis module for the automated dispensing procedure. The procedure is fully software based. The data of required activity for each PET-CT facility is given in the software. Then it automatically calculates the required volume for each vial. At first, the system's integrated dose calibrator determined the overall activity.

Fig. 2.: Automated CLIO dispensing unit at NINMAS

Then addition of required volume is each vial was done the dispensing unit automatically. A detailed digital batch record was created for traceability with the information's of dispensed volume and activity in each vial. The vial movements were carried out by using robotic manipulators in a completely closed and protected lead shielded cabinet. The similar distances were maintained to record exposed radiation levels once more, and staff exposure was measured using the same TLD badges and pocket dosimeters set up that is used for manual dispensing. For each dispensing procedure, observations were taken over ten times for all operational and safety parameters, such as vial preparation time, number of dispensed doses in each cycle, ambient exposed radiation doses, personal dosimeter reading, and mistake rates. Percentage changes between manual and automated dispensing were calculated to assess improvements in efficiency, radiation protection, and operational reliability. All dispensed procedures complied with International Atomic Energy Agency (IAEA) radiation safety protocols, Good Manufacturing Practice (GMP) for radiopharmaceuticals, and the institution's internal safety protocols.

3. Results and Discussion

The ambient radiation exposures during manual and automated dispensing using the CLIO system were compared at different distances from the [^{18}F] FDG dispensing source. During standard [^{18}F] FDG dose preparation and dispensing, measurements were made with calibrated survey meters placed at close contact (30 cm), 1 meter, and 2 meters from the dispensing site.

Table 1. Ambient Radiation Dose Rate (μSv/h) at Varying Distances from Dispensing Source

Distance from Dispensing Point	Manual Dispensing			CLIO Automated Dispensing		
	Min. (μSv/h)	Max. (μSv/h)	Avg±SD (μSv/h)	Min. (μSv/h)	Max. (μSv/h)	Avg±SD (μSv/h)
Close Contact (~30 cm)	40	50	45.0±2.9	8	10	9.0±0.6
1 meter	15	20	17.5±1.4	2	3	2.5±0.3
2 meters	4	5	4.5±0.3	0.2	0.5	0.15±0.09

Ambient doses showed a marked reduction in radiation exposure at all evaluated distances when using the CLIO automated dispensing system compared to the manual method. At close contact (~30 cm), the average dose rate decreased from 45.0±2.9 μSv/h during manual dispensing to 9.0±0.6 μSv/h with CLIO. At 1 m, values fell from 17.5±1.4 μSv/h to 2.5±0.3 μSv/h, and at 2 m from 4.5±0.3 μSv/h to 0.15±0.09 μSv/h. These findings indicate that automation with integrated lead shielding substantially reduces ambient radiation fields, particularly at close working distances, thereby improving occupational safety in the dispensing site.

Table 2. Average Absorbed Radiation Dose to Staff Measured by TLD and Pocket Dosimeter

Dosimeter Type	Manual Dispensing (μSv/day)	CLIO Dispensing (μSv/day)	% Reduction
TLD Badge (whole body)	<0.05	<0.05	No significant change (below detection limit)
Pocket Dosimeter	30	10	66.7%

Personal dose monitoring showed a remarkable decrease in recorded exposure when using the CLIO automated dispensing system. Pocket dosimeter measurements decreased from 30 μSv/day during manual dispensing to 10 μSv/day with automation, corresponding to a 66.7% reduction. Whole-body TLD badge readings remained below 0.05 μSv/day for both methods, indicating no remarkable difference within the detection limits of the monitoring system. These results highlight the role of automation in substantially lowering real-time occupational exposure while maintaining negligible whole-body dose levels.

Tab. 3. Comprehensive Comparison of Manual vs. CLIO automated Dispensing

Parameter	Manual Dispensing	CLIO Dispensing	Remarks
Vial preparation	2.0 ± 0.5 min	1.0 ± 0.2 min	↓ 50% Quicker in CLIO
Persons required	3	2	↓ 33.3% Less manpower in CLIO
Documentation	Manual	Digital batch logs	Less man -made error
Labelling	Handwritten	Automated barcoding	Less man -made error
QC delay post-preparation	Manual process (~20 min)	Digital data records	Maintained QA
Dose reproducibility (variation %)	±6.0%	±1.5%	↑ More precise in controlled volume
On-time dispensing (%)	~82%	~97%	↑ 18.3% Improved on-time delivery

After the implementation of CLIO automated dispensing system, there were noticeable improvements in operational performance of dispensing unit. With automation, the average time required for preparing a vial was cut in half, from 2.0 ± 0.5 minutes to 1.0 ± 0.2 minutes. A 33.3% reduction in required persons was done, as the number of staff members in every cycle dropped from three to two. Digital data records and automatic barcoding replaced manual and handwritten process for documentation and labelling, removing man-made errors and enhancing traceability. With the help of digital data records, quality control delays related to manual data entry (around 20 minutes) were eliminated, enabling synchronized batch clearing. As a result of improved volume control, dose reproducibility in dispensing vial increased from a variance of ±6.0% to ±1.5%. Compliance with on-time delivery rose from about 82% to 97%, representing an 18.3% improvement in delivery.

The outcomes of this study show that introduction of the automated CLIO system to replace manual [^{18}F] FDG dispensing led to significant improvements in workflow uniformity, efficiency in operations, and radiation safety. All distances from the dispensing unit showed a remarkable decrease in ambient absorbed radiation doses, with close distance (~30 cm) showing the largest relative decrease. The integrated lead shielding, closed [^{18}F] FDG dispensing and handling site, and robotic dose fractionation of the CLIO system, which together minimize radiation scatter and operator exposure, are responsible for this decrease [16,20]. These observations are same as the previous studies that showed that automated dispensing of radiopharmaceuticals dramatically lowers ambient absorbed doses without sacrificing efficiency [21]. Significantly lower radiation exposure for employees and increased operational effectiveness during regular radiopharmaceutical production were the study's main findings. The beneficial impact of automation is further enriched by personal dosimeter and TLD badge readings. Comparing CLIO to manual dispensing, pocket dosimeter findings showed a 66.7% decrease in daily operator exposure, even while whole-body TLD badge readings for both procedures remained below the detection limit. Due to frequent handling of highly active vials, extremity exposure has been observed as a major occupational hazard in manually vial dispensing [22]. The findings observed decrease in real-time recorded doses supports automation as a successful radiation protection measure and is consistent with the ALARA principle.

Operational indicators of performance showed significant improvements in procures in addition to exposed radiation safety. The average time required to prepare a dose per vial was cut in half, and a third fewer staffs were needed for each dispensing cycle. Automated barcoding and digital batch records replaced handwritten labels and paper-based records, improving traceability and lowering the possibility of man-made error. This is same as the findings from other facilities where automation has improved GMP compliance and made regulatory audits easier by supplying digital batch records [23,24]. The batch

release procedure was further expedited by the removal of manual QC paperwork delays, which allowed for prompter and more synchronized dose transmission.

With automation of dispensing, volume fluctuation decreased from ±6.0% in the manual process to ±1.5%, representing a significant improvement in dose repeatability. Since under- or over-administration can affect the on-time delivery of radiopharmaceuticals to all PET-CT facilities which is very important for both diagnostic accuracy and patient safety [25]. The automated procedure's capacity to reliably deliver scheduled vial dispensing with little operator interaction is reflected in the improved repeatability seen here. Lastly, the percentage of deliveries that were done on time rose from about 82% to 97%. Since ^{18}F, radio-isotope has a half-life of 110 minutes, prompt delivery is crucial to ensure sufficient activity at injection time, particularly for PET-CT facilities that are farther away from the production site. Increases in delivery reliability improve patient throughput and overall service efficiency by minimizing decay-related losses and reducing schedule conflicts [26]. Overall, the findings support the notion that incorporating an automated dispensing system into a centralized radiopharmaceuticals dispensing unit maximizes operational efficiency and adherence to quality standards while minimizing occupational radiation exposure. These results are in line with the expanding worldwide trend of nuclear medicine facility automation, which allows for the simultaneous achievement of operational effectiveness and worker safety without compromising product quality [27].

4. Conclusions

At NINMAS, the installation of the CLIO automated dispensing system for the dispensing of [^{18}F] FDG resulted in significant decreases in occupational radiation exposure, increased workflow efficiency, and better dosage preparation accuracy. Automation preserved product quality while reducing manual handling, increasing on-time delivery rates, and improving documentation correctness. In summary, the CLIO automated dispensing system at NINMAS showed efficacy in lowering radiation exposure for employees and enhancing operational effectiveness in routine production of radiopharmaceuticals, all while upholding high standards of quality.

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