

Radiosynthesis and Quality Control of (¹⁸F) PSMA-1007 at the Cyclotron Facility of National Institute of Nuclear Medicine and Allied Sciences (NINMAS) for Diagnosis of Prostate Cancer

¹Md. Jashim Uddin, ²Mohammad Anwar-Ul-Azim, ¹Sanchoy Chandra Biswasarma, ¹Md. Saiful Islam, ¹Sanjida Islam, ¹Mustafa Mamun, ¹Ferdoushi Begum, ¹Md. Nahid Hossain, ¹Md. Shohag Mia, ¹Hasan Mehdi, ¹Md. Nur-E-Alam Siddiquee, ¹Muhtasin Kadir

¹ National Institute of Nuclear Medicine and Allied Sciences (NINMAS), Bangladesh Atomic Energy Commission (BAEC), Block-D, BSMMU campus, Shahbag, Dhaka, Bangladesh.

² Planning & Development Division, Bangladesh Atomic Energy Commission (BAEC).

Correspondence Address : Dr. Mohammad Anwar-Ul-Azim, Principal Scientific Officer, Planning & Development Division, BAEC, Sher-E-Bangla Nagar, Dhaka Email: anwarri79@gmail.com

ABSTRACT

Radiolabeled tracers targeting prostate-specific membrane antigen (PSMA) have revolutionized PET imaging for prostate cancer diagnosis. Here, we present the inaugural production and quality control assessment of (¹⁸F) PSMA-1007 at the National Institute of Nuclear Medicine and Allied Sciences (NINMAS), Bangladesh. The synthesis, conducted via a one-step procedure, yielded remarkable radiochemical yields (46.85%) with synthesis time 40 minutes. Quality control measures adhered to European Pharmacopoeia standards, enabling clinical deployment across Nuclear Medicine and PET-CT centers in Bangladesh. This pioneering effort marks a significant advancement in prostate cancer imaging within the region.

Keywords: (¹⁸F) PSMA-1007; prostate cancer; PET imaging; quality control; Bangladesh

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INTRODUCTION

Prostate-specific membrane antigen (PSMA)-PET has emerged as a superior imaging modality for prostate cancer diagnosis, particularly in cases with low PSA levels (1-3). Though gallium-68-labeled PSMA-targeting radioligands are prevalent, their production capacity is limited with the cyclotron (4-6). Hence, there's a growing interest in radiofluorinated PSMA ligands (6,7). Notably, (¹⁸F) PSMA-1007 has shown promise in PET imaging of prostate cancer (8,9). Although widely adopted elsewhere, its synthesis and clinical use in Bangladesh were pending. This study bridges the gap by detailing the inaugural production and quality control processes of (¹⁸F) PSMA-1007 at NINMAS.

METHODS

(¹⁸F) Fluoride was produced by the ¹⁸O (p, n)¹⁸F nuclear reaction with proton irradiation to 2.5 mL (¹⁸O) H₂O (98% abundance, Huayi Technology, China) using a cyclotron with 18/9 MeV energy (Cyclone®-18/9, IBA, Germany). The synthesis of (¹⁸F) PSMA-1007 was performed using a single use cassette-type Sythera® autosynthesizer (IBA, Germany, Figure-1) via direct substitution. Radiolabeling was conducted using precursor PSMA-1007 and Tetrabutylammonium hydrogen carbonate (TBAHCO₃-) solution (ABX Germany, Figure-2), with quality control tests performed according to established protocols including gas chromatography, potentiometry, limulus amebocyte lysate test, bubble point test, and thin layer chromatography.

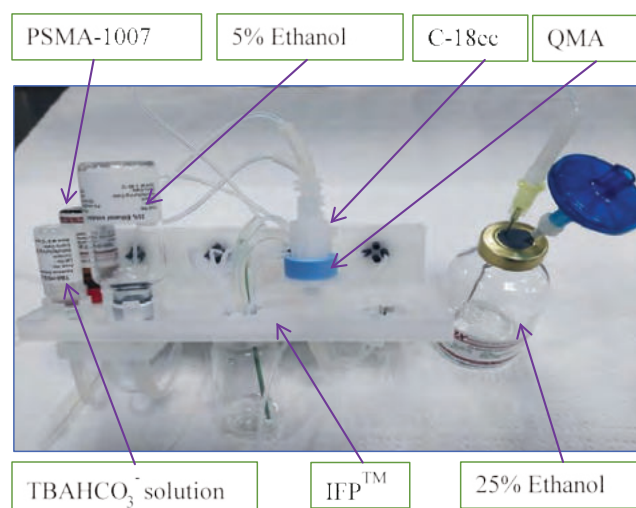


Figure-1: Setup of the Ancillaries, Reagent & Integrated Fluidic Processor (IFP)

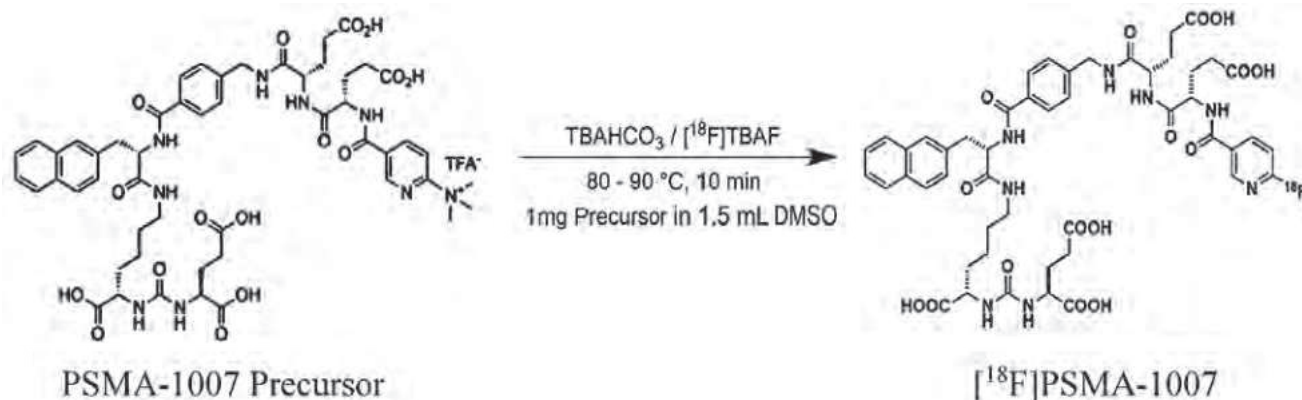


Figure-2: Synthesis [¹⁸F] PSMA-1007 by direct nucleophilic substitution reaction.

RESULTS

(¹⁸F) PSMA-1007 was successfully synthesized with radiochemical yields of 46.85% and synthesis time 40 minutes, meeting European Pharmacopoeia standards.

Quality control assessments verified the formulation's compliance with safety and efficacy criteria (Table-1), facilitating its clinical utility for prostate cancer detection in Bangladesh.

Table-1: Quality control results summary of synthesized (¹⁸F) PSMA-1007 at NINMAS

| Quality parameter | Specification | Results | Comment |
|---------------------------------------|-----------------------------|------------------------------|---------|
| Appearance | Colorless/Clear/No particle | Colorless/Clear /No particle | Pass |
| Bacterial Endotoxin Test | < 17.5 EU/mL | 0.2024 EU/mL | Pass |
| p^H | 4.5-8.5 | 6.5 | Pass |
| Radiochemical Purity (TLC) | > 95% | 96.1% | Pass |
| Half Life | 105-115 min | 108 min | Pass |
| Gamma-ray Energy | 511 keV | 511eV | Pass |
| Filter Integrity Test | > 50 psi | 62 psi | Pass |
| Residual DMSO | < 5000 ppm | 100 ppm | Pass |
| Residual Ethanol | < 5000 ppm | 256 ppm | Pass |
| Sterility test (FTM & TSB) | No turbidity | No Growth | Pass |

DISCUSSION

Prostate-specific membrane antigen (PSMA) plays a pivotal role in prostate cancer (PCa) imaging and therapy due to its high expression in cancer cells. PSMA-labeled radiotracers enable precise detection of PCa lesions, aiding in staging, restaging, and treatment response assessment (10). (¹⁸F)-labeled PSMA-targeted PET imaging compounds offer significant advantages over (⁶⁸Ga)-PSMA. They enable facilitated delivery from distant suppliers, expanding accessibility especially in smaller hospitals without onsite ⁶⁸Ga-generators, potentially leading to cost savings. (¹⁸F)-labeled radiotracers provide higher positron yield and lower energy, reducing image noise and improving contrast resolution for enhanced lesion detection. Their longer

half-life ensures improved imaging protocols and flexibility in study design, while avoiding regulatory restrictions on onsite production or limited cyclotron access. These advantages make (¹⁸F)-labeled compounds significant in optimizing prostate cancer imaging and facilitating broader clinical adoption (11). Apart from these issues, cyclotron facility of NINMAS is limited in producing ⁶⁸Ga because we lack the necessary targets and related facilities. As a result, we chose to synthesize (¹⁸F) PSMA-1007 instead. The successful synthesis and quality control assessment of (¹⁸F) PSMA-1007 at NINMAS demonstrate the feasibility and efficacy of implementing this novel radiotracer for prostate cancer imaging in Bangladesh. The efficient one-step synthesis process, coupled with stringent quality control

measures, ensures the formulation's safety and efficacy for routine clinical use across the region. This achievement underscores the institution's commitment to advancing molecular imaging technologies and enhancing patient care in Bangladesh.

CONCLUSION

The pioneering synthesis and quality control evaluation of (¹⁸F) PSMA-1007 at NINMAS mark a significant milestone in advancing prostate cancer imaging in Bangladesh.

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