**2nd ProtoTera PhD Students Workshop** – C$^2$TN, Lisbon – 09 to 11 October 2024

# Fully Automated Synthesis of Copper-61-based Radiopharmaceuticals for Prostate Cancer Detection

Abstract

Diana Rodrigues[1], Alexandra Fonseca[2], Sérgio do Carmo[1,2], José Sereno[1], Célia Gomes[3], Antero Abrunhosa[1,2]

1 – ICNAS/CIBIT — Instituto de Ciências Nucleares Aplicadas à Saúde/Coimbra Institute for Biomedical Imaging and Translational Research, Universidade de Coimbra, Pólo das Ciências da Saúde, Coimbra, Portugal
2 – ICNAS Pharma, Edifício do ICNAS, Polo das Ciências da Saúde, Coimbra, Portugal
3 – iCBR — Coimbra Institute for Clinical and Biomedical Research, Faculty of Medicine, University of Coimbra, Portugal

**Background:** Considered incurable at advanced stages, prostate cancer (PCa) remains a major health concern. Therefore, new strategies for early diagnosis and effective therapies are urgently needed to overcome the poor prognosis of patients. Nuclear imaging techniques, particularly positron emission tomography (PET), have played a significant role in addressing this issue in recent years. Considering the advantageous physical decay properties of copper-61, compared to those of the current PET gold-standard gallium-68, we describe a fully automated synthesis process of a $^{61}$Cu-based radiopharmaceutical - [$^{61}$Cu]Cu-NODAGA-PSMA-I&T - for prostate specific membrane antigen (PSMA) PET imaging in PCa.

**Methodology:** The fully automated purification of copper-61 and subsequent radiolabeling reaction were accomplished by using two disposable cassette kits and two IBA Synthera® Extension modules. The purified radiolabeled compound obtained at the end of synthesis was then subjected to quality control tests to assess its radiochemical purity (iTLC + HPLC), pH and radionuclidic identity. The stability of the radiopharmaceutical was also

evaluated over a period of 6 h. The specificity and binding affinity of [$^{61}$Cu]Cu-NODAGA-PSMA-I&T for PSMA were evaluated in vitro using the LNCaP (PSMA+) and DU145 (PSMA-) prostate cancer cell lines. PET/MR imaging studies were performed in LNCaP tumor-bearing mice.

**Results:** The developed automated process was found to be effective, as no significant loss of radioactivity was observed in any of the components of the radiolabeling kit. The quality of [$^{61}$Cu]Cu-NODAGA-PSMA-I&T was demonstrated, with all the quality control parameters meeting the considered guidelines. The radiopharmaceutical showed excellent stability over time, and the in vitro uptake studies confirmed its specificity for PSMA. In vivo PET imaging showed clear tumor uptake up to 4 h post injection, along with renal clearance, and no significant uptake in non-targeted organs.

**Conclusions:** Our results demonstrate the feasibility of the implemented automated process, which yields high-quality [$^{61}$Cu]Cu-NODAGA-PSMA-I&T and can be easily implemented in any research center equipped with a cyclotron optimized for fluorine-18 production. The simple, cost-effective and reliable method for copper-61 purification and NODAGA-PSMA-I&T radiolabeling herein presented represents a significant advance in the radiopharmacy field, encouraging the wider use of copper-61 in clinical practice as an alternative to the outdated gallium-68.