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[^{99m}Tc][Tc(N)(PNP3OH)]-PSMAi: a new Cost-Effective Candidate for PCa SPECT Diagnosis

N. Salvarese[1], C. Gobbi[1], J. Kleynhans[2], I. Hawala[3], S. Ghiani[4], A. Maiocchi[5], F. Cleeren[2], C. Bolzati[1]*

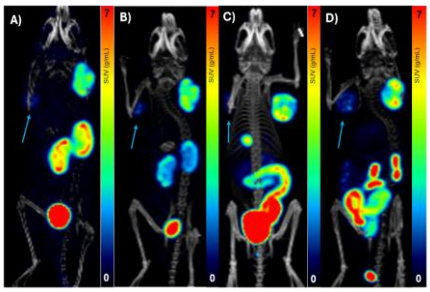
[1]Institute of Condensed Matter Chemistry and Energy Technologies-ICMATE-CNR, Padova, Italy; [2]Laboratory for Radiopharmaceutical Research, Dep of Pharmacy and Pharmacology Science, KU Leuven, Belgium; [3]Dipartimento di Biotecnologie Molecolari e Scienze per la salute, Università degli Studi di Torino, Italy; [4]Bracco Research Centre, Bracco Imaging SpA, Torino, Italy; [e]Bracco SpA, Milano, Italy

nicola.salvarese@*cnr.it*

Aim. While [^{68}Ga]Ga- and [^{18}F]F-labeled PSMA inhibitors (PSMAi) have revolutionized the management of prostate cancer (PCa) patients, the high cost and limited availability of PET equipment remain a challenge in patient care in remote regions. The development of technetium-99m (^{99m}Tc) based SPECT tracers could provide a more accessible and cost-effective alternative for global clinical implementation. Although the [^{99m}Tc]Tc-MIP-1404 complex (RoTecPSMA®, ROTOP Pharmaka GmbH) has recently been approved in the UK and Switzerland as the first PSMA-SPECT tracer for PCa imaging and detection, many of the proposed agents possess important limitations with lower sensitivity to micrometastases and suboptimal pharmacokinetics that results in high background noise and off-target uptake.

Exploiting the chemical properties of the recently reported [^{99m}Tc][TcN(PNP3OH)]-synthon (PNP3OH= $[(HOCH_2)_2PCH_2CH_2]_2NCH_2CH_2OCH_3$),[1] we developed a new radioligand targeting PSMA. This tracer was designed to improve biological properties and the detection of primary tumors and metastases by SPECT imaging.

Materials and Methods [^{99m}Tc][Tc(N)(PNP3OH)]-PSMAi was prepared (RCP > 95%; molar activity 30 GBq/µmol). Stability and cell-specific uptake were assessed in relevant PSMA(+)/PSMA(-) cells. The complex was preclinically evaluated and compared with clinically tested [^{99m}Tc][Tc-HYNIC]-iPSMA.[2]



	[^{99m}Tc]Tc-EDDA/HYNIC-iPSMA		[^{99m}Tc]Tc-PNP3OH-cysPSMA	
	1 h	4 h	1 h	4 h
Kidneys	**7.7 ± 1.7**	**2.9± 0.6**	**1.0 ± 0.1**	**0.4 ± 0.0**
Liver	0.2 ± 0.1	0.1 ± 0.1	0.6 ± 0.5	0.2 ± 0.1
PSMA(+)	3.8 ± 0.7	3.7 ± 0.7	**5.7 ± 0.5**	**5.4 ± 0.7**
PSMA(-)	1.4 ± 0.2	1.3 ± 0.1	**1.0 ± 0.1**	**1.2 ± 0.3**

Fig 1. Fused µSPECT/CT images of [^{99m}Tc]Tc-EDDA/HYNIC-iPSMA at 1 h (A) and 4 h (B) p.i. and of [^{99m}Tc]Tc-PNP3OH-cysPSMA at 1 h (C) and 4 h (D) p.i. The arrows indicate the location of the PSMA-negative tumors . Representative radio-chromatogram of urine sample (E) taken at 1 h p.i. Table summarized the quantitative SUVmax data obtained from µSPECT/CT images (N=3 per time-point).

Results [^{99m}Tc][Tc(N)(PNP3OH)]-PSMAi demonstrated high stability and specific accumulation in PSMA(+) cells. Animal studies (Fig.1) show a superior positive-to-negative tumor ratio (4.37) compared to [^{99m}Tc][Tc-HYNIC]-iPSMA (2.87). Faster clearance from nontarget organs was also observed. No uptake was evident in the spleen and salivary glands; kidney accumulation was negligible at 1 h and undetectable at 4 h after injection.

Conclusions. With its high tumor uptake and favorable pharmacokinetics [^{99m}Tc][Tc(N)(PNP3OH)]-PSMAi is a promising cost-effective candidate for large-scale clinical PCa screening.

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[1] Bolzati, C. *et al. Mol. Pharm.* **19**, 876−894 (2022); [2] Ferro-Flores, G. *et al. Nucl. Med. Biol.* **48**, 36–44 (2017).