Popular Science

नाभिकीय चिकित्सा में रिसेप्टर-लक्षित थेरेनोस्टिक्स: वर्तमान स्थिति एवं संभावित भावी नैदानिक अनुप्रयोग

Receptor Targeted Theranostics in Nuclear Medicine: Current Status & Potential Future Clinical Applications

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Modern health care is moving towards precision through significant development of theranostic radiopharmaceuticals for cancer diagnosis and therapy. Nuclear medicine stands out distinctly due to its ability to provide precise functional and physiological details regarding a disease like cancer. This significant benchmark is not possible without the substantial contribution of nuclear sciences. It is a field where the gift of nuclear technology is translated into medical tools for imaging and targeted treatment at the molecular level. At the Radiation Medicine Centre, BARC, an amalgamation of basic nuclear sciences and clinical nuclear medicine, is enabling precision cancer care with the help of receptor-targeted radiopharmaceuticals (Fig.1).

Diseased cells, especially cancer cells, overexpress receptors that can act as molecular targets. The receptor-targeted radiopharmaceuticals are specifically designed for binding to these selective targets at the molecular level. The highly sensitive molecular imaging, like PET/CT and SPECT/CT, can be performed when these targeting molecules are labeled with suitable radioisotopes like [a] Gallium-68 (^{68}Ga) & Fluorine-18 (^{18}F) for PET, and [b] Technetium-99m (^{99m}Tc) & Indium-111(^{111}In) for SPECT. Additionally, same molecular target when radiolabelled with radionuclide like Lutetium-177 (^{177}Lu) (beta emitter) & Actinium-225 (^{225}Ac) (Alpha emitter) can deliver therapeutic effect to tumor sites. This approach of clinical diagnosis, treatment, and monitoring of diseases using related radio pharmaceuticals enables personalized patient management and is popularly known as theranostics (Fig.2).

Somatostatin Receptor Radionuclide Therapy (PRRT) for the Treatment of Neuroendocrine Tumors

Peptide receptor radionuclide therapy (PRRT) for the treatment of neuroendocrine tumors (NET) is one of the significant benchmarks in receptor targeted theranostics. In this strategy, the somatostatin receptor expression can be visualized through PET/SPECT by radiolabeling somatostatin analog peptide, and this information can be used to plan targeted therapy using therapeutic radionuclides like Lutetium-177 (beta emitter), Actinium-225 (Alpha emitter). PRRT delivers radiation selectively to tumor cells, thereby minimizing exposure to the surrounding healthy cells. The radionuclide selection can be done according to the tumor size, and disease status.

A large number of patients with advanced or metastatic neuroendocrine tumors have significantly benefitted from PRRT at the Radiation Medicine Centre (RMC), utilizing both indigenous and imported ^{177}Lu and ^{225}Ac. More than 10,000 successful PRRTs have been administered at the Centre over last 16 years and is committed to serving many more in the future (Fig.3).

PSMA targeted Radioligand Therapy (PRLT) in Metastatic Castrate Resistant Prostate Cancer

PRRT paved the path for prostate-specific membrane antigen (PSMA)-targeted theranostics, which improved prostate cancer management at the RMC significantly. The prostrate specific membrane antigen (PSMA) is overexpressed in prostate cancer. Radiopharmaceutical targeting PSMA enables PET imaging for the spread of disease and targeted therapy for advanced metastatic prostate cancer patient (Fig.4).

Fig.1: Translation of Nuclear science & technology to Clinical Nuclear Medicine showing the pathway from radioisotope production to patient care.

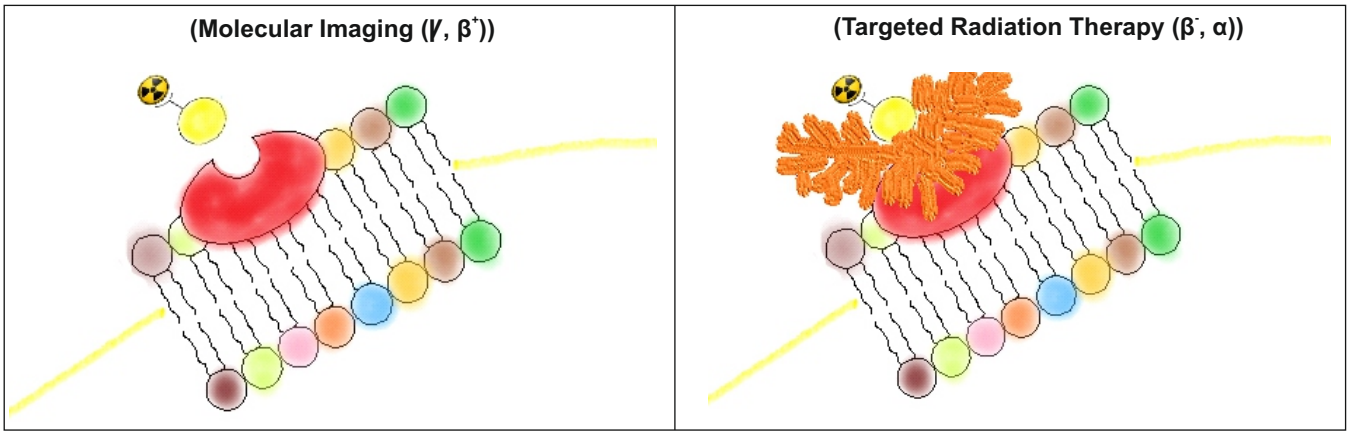

Fig.2: Diagrammatic representation of principle of receptor-targeted theranostics illustrating molecular targeting with radiolabelled ligands for imaging and therapy.

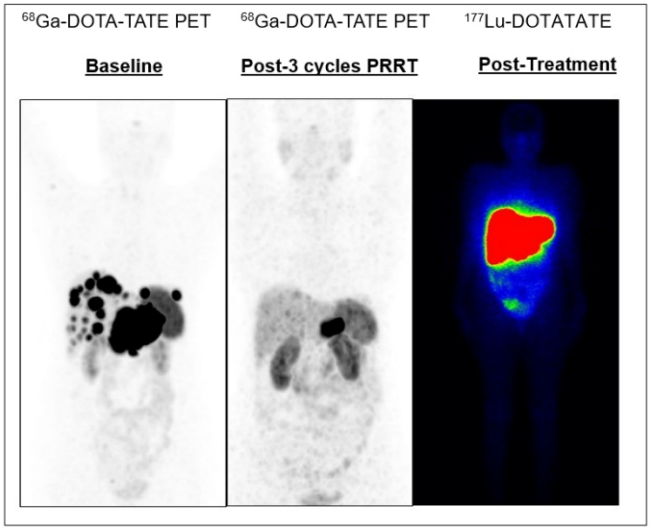

Fig.3: Somatostatin receptor based ^{68}Ga-DOTA-TATE PET and targeted PRRT in a patient of metastatic neuroendocrine tumor showing excellent response to PRRT. The ^{177}Lu-DOTATATE post-treatment planar gamma camera image (right column) showing intense uptake of therapeutic dose in tumour tissue.

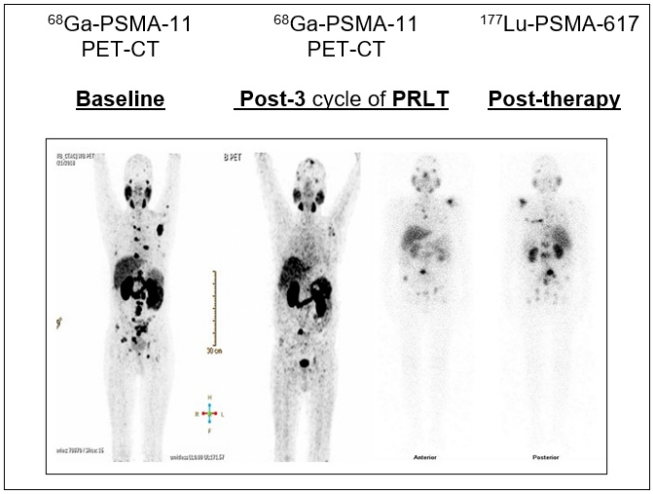

Fig.4: PSMA PET imaging demonstrating metastatic prostate cancer, enabling targeted radionuclide therapy with ^{177}Lu-PSMA-617 and showing excellent treatment response in a patient of Metastatic Castrate Resistant Prostate Carcinoma.

FAPI-targeted Radioligand Therapy

Currently, fibroblast activation protein inhibitors (FAPI) based radio pharmaceuticals are proving to be promising agents targeting cancer-associated fibroblasts in the tumor microenvironment. FAPI-based radiopharmaceuticals represent an expanding frontier in nuclear medicine theranostics by targeting a wide range of tumor type (Fig.5).

Image-based Dosimetry in Nuclear Medicine Theranostics

Advanced imaging systems and quantitative techniques that support diagnosis and therapy planning are strong pillars of modern nuclear medicine. They play a crucial role in molecular imaging and therapy undertaken by the state-of-art imaging facility such as PET/CT and SPECT/CT with receptors targeted radiopharmaceuticals.

In addition to the sensitive detection of disease with radiopharmaceutical distribution and post-radionuclide therapy evaluation, the personalized treatment planning with improved safety and effectiveness of the radionuclide therapy is achieved by dosimetric studies. Dosimetry enables radiation dose estimation to the tumor lesions and normal organs (Fig.6).

A true interdisciplinary effort has led to the development and clinical translation of receptor-targeted theranostics. Multiple diverse domains of nuclear sciences and biomedical research have contributed to this success, beginning with the production of medical radioisotopes using nuclear technology, and the design of receptor-targeted molecules is achieved by advanced molecular labeling and radiopharmaceutical chemistry. Once designed, they are synthesized and subsequently labeled in specialized hospital radiopharmacy. The clinical translation of these radiopharmaceuticals is done through molecular imaging and targeted radionuclide therapy

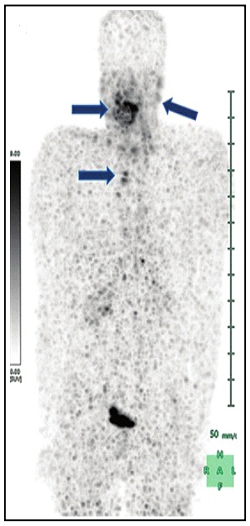

Fig.5: ^{68}Ga-FAPI-4 PET imaging showing uptake by the cancer-associated fibroblasts within the tumor microenvironment.

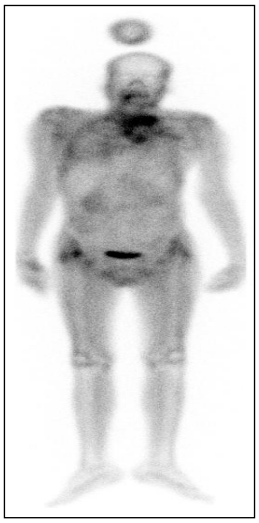

Fig.6: Image Based Dosimetry for dose estimation of patient treated with ^{177}Lu-FAPI- 2286.

in Nuclear Medicine. The Radiation Medicine Centre stands out uniquely by integrating nuclear physics, chemistry, biology, and clinical medicine, and thereby contributing to advancing precision health care.

The Radiation Medicine Centre, with its pioneering and high-volume extensive clinical and theranostic services to patients with neuroendocrine tumors and prostate cancer by means of PRRT and PSMA-based PRLT respectively, continuously strives to contribute significantly to the development of receptor based National level Theranostics in Nuclear medicine. Exploring emerging tracers such as FAPI is an advanced step towards this end. Such efforts significantly improve the quality of life of many cancer patients of the country.

References

[1] Basu S, Chakraborty S, Parghane RV, Kamaldeep, Ranade R, Thapa P, et al. One decade of 'Bench-to-Bedside' peptide receptor radionuclide therapy with indigenous [^{177}Lu] Lu-DOTATATE obtained through 'Direct' neutron activation route: lessons learnt including practice evolution in an Indian setting. Am J Nucl Med Mol Imaging. 2020 Aug 25;10(4):178-211.

[2] Basu S, Parghane RV, Kamaldeep, Chakrabarty S. Peptide Receptor Radionuclide Therapy of Neuroendocrine Tumors. Semin Nucl Med. 2020 Sep;50(5):447-464.

[3] Suman S, Parghane RV, Joshi A, Prabhash K, Bakshi G, Talole S, Banerjee S, Basu S. Therapeutic efficacy, prognostic variables and clinical outcome of ^{177}Lu-PSMA-617 PRLT in progressive mCRPC following multiple lines of treatment: prognostic implications of high FDG uptake on dual tracer PET-CT vis-à-vis Gleason score in such cohort. Br J Radiol. 2019 Dec;92(1104):20190380.

[4] Suman S, Parghane RV, Joshi A, Prabhash K, Talole S, Basu S. Combined ^{177}Lu-PSMA-617 PRLT and abiraterone acetate versus ^{177}Lu-PSMA-617 PRLT monotherapy in metastatic castration-resistant prostate cancer: An observational study comparing the response and durability. Prostate. 2021 Nov;81(15):1225-1234.

[5] Ravada SK, Parghane RV, Basu S. Dichotomous Uptake Pattern on [^{18}F] F-FDG and [^{68}Ga] Ga-DOTA-FAPI-04 PET/CT in Lytic, Sclerotic and Marrow Metastatic Skeletal Lesions in Medullary Thyroid Carcinoma. Clin Nucl Med. 2025 Nov 3. doi: 10.1097/RLU.0000000000006206.