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Review Article

Nuclear Medicine in Cancer: Advances, Applications and Future Perspectives

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ABSTRACT

Nuclear medicine has emerged as a transformative discipline in oncology, enabling precise diagnosis, staging, and treatment of various malignancies through the use of radiopharmaceuticals. By combining functional imaging with molecular targeting, it offers a unique advantage over conventional anatomical imaging techniques. Recent advancements, including hybrid imaging systems, novel radiotracers, and targeted radionuclide therapy, have significantly improved clinical outcomes. This review discusses the fundamental principles, current applications, recent innovations, and future prospects of nuclear medicine in cancer management. Emphasis is placed on theranostics, personalized medicine, and emerging technologies that are reshaping the landscape of oncology.

INTRODUCTION

Cancer continues to pose a major global health burden, accounting for millions of deaths each year and significantly affecting quality of life. According to the World Health Organization, cancer is one of the leading causes of mortality worldwide, with an increasing incidence driven by aging populations, environmental factors, and

lifestyle changes (WHO, 2023). The growing complexity of cancer biology has created an urgent need for advanced diagnostic and therapeutic approaches that go beyond conventional methods. Traditional imaging techniques such as computed tomography (CT) and magnetic resonance imaging (MRI) primarily provide anatomical details, which, although valuable, may not always reflect the underlying biological activity of

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tumors. In contrast, nuclear medicine offers a functional and molecular perspective by visualizing physiological processes such as metabolism, receptor expression, and cellular proliferation. This capability allows for earlier detection of malignancies and more accurate characterization of disease progression (Jadvar, 2016). Nuclear medicine is based on the use of radiopharmaceuticals—compounds labeled with radioactive isotopes that selectively target specific tissues or biochemical pathways. Once administered, these agents emit radiation that can be detected by specialized imaging systems, enabling clinicians to observe biological processes in real time. Techniques such as positron emission tomography (PET) and single-photon emission computed tomography (SPECT) have become indispensable tools in oncology, particularly when integrated with hybrid systems like PET/CT and PET/MRI, which combine functional and structural imaging for enhanced diagnostic precision (Gambhir, 2002). One of the most significant contributions of nuclear medicine to oncology is its ability to detect cancer at a very early stage, often before structural changes become apparent. For instance, the radiotracer fluorodeoxyglucose (FDG), widely used in PET imaging, accumulates in cancer cells due to their increased glucose metabolism—a hallmark of many tumors. This allows for sensitive detection of primary tumors as well as metastatic lesions, thereby improving staging accuracy and treatment planning (Boellaard, 2009). In addition to diagnosis, nuclear medicine plays a critical role in evaluating therapeutic response and disease prognosis. Functional imaging can reveal metabolic changes in tumors shortly after treatment initiation, providing early insights into treatment effectiveness. This is particularly valuable in modern oncology, where personalized treatment strategies are increasingly emphasized. Furthermore, the field has evolved beyond

imaging into targeted therapy through the development of radionuclide-based treatments. This approach enables the delivery of cytotoxic radiation directly to cancer cells while minimizing damage to surrounding healthy tissues. The concept of “theranostics”—a combination of therapy and diagnostics—represents a paradigm shift in cancer management, aligning closely with the goals of precision medicine (Baum & Kulkarni, 2012). Despite its many advantages, the integration of nuclear medicine into routine clinical practice is not without challenges, including issues related to cost, infrastructure, and radiation safety. Nevertheless, ongoing advancements in radiopharmaceutical development, imaging technology, and computational analysis continue to expand its clinical applications. Overall, nuclear medicine has transformed the landscape of oncology by providing deeper insights into tumor biology and enabling more accurate, individualized patient care. As research continues to advance, its role is expected to grow further, contributing significantly to improved cancer diagnosis, treatment, and long-term management.

2. Principles Of Nuclear Medicine In Oncology

Nuclear medicine is grounded in the concept of visualizing physiological and biochemical processes within the body rather than relying solely on structural imaging. This functional approach is particularly valuable in oncology, as malignant transformation is often associated with early molecular and metabolic alterations that precede anatomical changes (Jadvar, 2016). By capturing these subtle biological events, nuclear medicine enables earlier detection, improved disease characterization, and more informed clinical decision-making. The foundation of nuclear medicine lies in the use of radiopharmaceuticals—compounds that combine



a radioactive isotope with a biologically active molecule. These agents are designed to selectively localize in specific tissues or bind to molecular targets associated with cancer. Once administered, the emitted radiation is detected by specialized imaging systems, allowing real-time visualization of biological activity within the body (Cherry et al., 2012).

2.1 Radiopharmaceuticals

Radiopharmaceuticals play a central role in both diagnostic and therapeutic applications of nuclear medicine. Each radiopharmaceutical consists of two key components: a radionuclide, which emits detectable radiation, and a targeting molecule, which directs the compound to specific cells or receptors. For diagnostic imaging, radionuclides such as technetium-99m, fluorine-18, and gallium-68 are commonly used due to their favorable physical properties, including appropriate half-lives and radiation energy profiles (IAEA, 2019). Among these, fluorine-18 labeled fluorodeoxyglucose (FDG) is one of the most widely utilized tracers in oncology. FDG acts as a glucose analogue and accumulates in metabolically active cells. Since cancer cells typically exhibit increased glucose metabolism—a phenomenon known as the Warburg effect—FDG uptake serves as a reliable marker for tumor detection and assessment (Boellaard, 2009). In addition to metabolic imaging, newer radiotracers have been developed to target specific molecular pathways, such as hormone receptors, cell proliferation markers, and tumor-specific antigens. This has significantly improved the specificity of nuclear imaging and supports the growing trend toward personalized medicine. For therapeutic purposes, radionuclides that emit cytotoxic radiation, such as iodine-131, lutetium-177, and yttrium-90, are commonly employed. These isotopes deliver targeted radiation to

malignant cells, causing DNA damage and subsequent cell death while minimizing exposure to surrounding healthy tissues (Dash et al., 2015). The choice of radionuclide depends on factors such as tumor type, size, and localization.

2.2 Imaging Modalities

The visualization of radiopharmaceutical distribution is achieved through advanced imaging technologies, primarily positron emission tomography (PET) and single-photon emission computed tomography (SPECT).

Positron Emission Tomography (PET) is a highly sensitive imaging modality that utilizes positron-emitting radionuclides such as fluorine-18. When positrons emitted from the radionuclide interact with electrons in the body, they undergo annihilation, producing two gamma photons that travel in opposite directions. These photons are detected simultaneously by the PET scanner, allowing precise reconstruction of tracer distribution (Cherry et al., 2012). PET is particularly advantageous in oncology due to its high spatial resolution and ability to quantify metabolic activity, making it a powerful tool for tumor detection, staging, and therapy monitoring.

Single-Photon Emission Computed Tomography (SPECT) employs gamma-emitting radionuclides such as technetium-99m. Although SPECT generally offers lower resolution compared to PET, it remains widely used due to its cost-effectiveness and accessibility. It is especially useful in applications such as bone scintigraphy and certain tumor imaging procedures (IAEA, 2019). The introduction of hybrid imaging systems, such as PET/CT and PET/MRI, has further enhanced the clinical utility of nuclear medicine. By combining functional imaging with anatomical detail, these systems allow for more

accurate localization of lesions and improved diagnostic confidence (Townsend, 2008).

2.3 Mechanism of Imaging and Signal Detection

Nuclear imaging involves a sequence of events beginning with the administration of a radiopharmaceutical, followed by its distribution and accumulation in target tissues. The emitted radiation is detected by specialized الأجهزة such as gamma cameras (for SPECT) or PET detectors. These systems use scintillation crystals that convert incoming radiation into light signals, which are then transformed into electrical signals and processed to create images. The intensity of the detected signal reflects the concentration of the radiotracer in a given region, providing insights into the underlying biological activity (Cherry et al., 2012). Clinically, areas of increased tracer uptake are referred to as “hot spots” and often indicate regions of high metabolic or biochemical activity, commonly associated with tumor tissue. In contrast, “cold spots” represent areas of reduced uptake and may correspond to necrotic or poorly perfused tissue.

2.4 Pharmacokinetics and Biodistribution

The pharmacokinetic behavior of radiopharmaceuticals plays a crucial role in determining image quality and diagnostic accuracy. After administration, these agents undergo distribution through the bloodstream, followed by selective uptake in target tissues based on factors such as receptor expression, metabolic activity, and regional blood flow (Wahl, 2002). Normal physiological uptake in organs such as the brain, liver, and kidneys must be carefully distinguished from pathological uptake to avoid diagnostic errors. Advances in quantitative imaging and kinetic modeling have enabled more precise assessment of tracer distribution,

improving the reliability of nuclear imaging in oncology.

2.5 Radiation Safety and Dosimetry

Despite the use of radioactive materials, nuclear medicine procedures are generally safe when performed under established guidelines. Diagnostic imaging typically involves low radiation doses, while therapeutic applications use higher doses that are carefully targeted to tumor tissues (IAEA, 2019). Dosimetry is a critical aspect of nuclear medicine, involving the calculation of radiation absorbed by different tissues. This ensures that therapeutic doses are optimized to maximize tumor control while minimizing toxicity to normal organs. Continuous advancements in dosimetric techniques and radiopharmaceutical design have contributed to improved safety profiles and treatment outcomes.

3. Applications In Cancer Diagnosis And Staging

Nuclear medicine has become an indispensable component of modern oncology, particularly in the areas of cancer detection, staging, and treatment monitoring. By providing functional and molecular information, it complements conventional imaging modalities and often reveals disease processes that may not yet be structurally apparent. This capability has significantly improved the accuracy of diagnosis and the effectiveness of clinical decision-making (Jadvar, 2016).

3.1 Early Detection of Cancer

One of the most valuable contributions of nuclear medicine is its ability to detect malignancies at an early stage. Cancer cells often exhibit altered metabolic activity, increased proliferation, and changes in receptor expression long before



physical changes become visible on anatomical imaging. Nuclear imaging techniques, particularly positron emission tomography (PET), can capture these early biological alterations. A widely used radiotracer in this context is fluorine-18 fluorodeoxyglucose (FDG), which acts as a glucose analogue. Due to the enhanced glycolytic activity of cancer cells—a phenomenon described as the Warburg effect—FDG accumulates preferentially in malignant tissues. This allows PET imaging to identify tumors with high sensitivity, even when they are small or not yet anatomically distinct (Boellaard, 2009). Early detection is especially important in cancers such as lung, colorectal, and lymphoma, where timely diagnosis can significantly improve survival outcomes. Moreover, nuclear medicine can help differentiate between benign and malignant lesions based on their metabolic characteristics, reducing the need for invasive diagnostic procedures (Wahl, 2002).

3.2 Tumor Staging and Restaging

Accurate staging is essential for determining the extent of disease and selecting the most appropriate treatment strategy. Nuclear medicine plays a crucial role in staging by providing whole-body imaging that can detect both primary tumors and distant metastases in a single examination. Hybrid imaging techniques such as PET/CT have greatly enhanced staging accuracy by combining metabolic and anatomical information. PET identifies areas of abnormal tracer uptake, while CT provides precise localization of these regions within the body. This integrated approach improves the detection of lymph node involvement and distant metastases, which are critical factors in cancer staging (Townsend, 2008). In addition to initial staging, nuclear medicine is also valuable in restaging—assessing disease progression or recurrence after treatment. For example, PET

imaging can distinguish between scar tissue and active tumor, which is often difficult using conventional imaging alone. This is particularly relevant in cancers such as lymphoma and head-and-neck malignancies, where post-treatment changes can complicate interpretation (Juweid & Cheson, 2006).

3.3 Evaluation of Treatment Response

Monitoring the effectiveness of cancer therapy is another area where nuclear medicine provides significant advantages. Traditional imaging methods typically rely on changes in tumor size to assess response, which may take weeks or months to become apparent. In contrast, nuclear imaging can detect changes in tumor metabolism shortly after treatment initiation. A decrease in FDG uptake on PET imaging often indicates a positive response to therapy, even before any reduction in tumor size is observed. This early assessment allows clinicians to modify treatment strategies if necessary, avoiding ineffective therapies and reducing unnecessary side effects (Weber, 2009). Functional imaging is particularly useful in evaluating response to chemotherapy, radiotherapy, and targeted therapies. It also plays an important role in clinical trials, where it is used as a biomarker to assess the efficacy of new anticancer agents.

3.4 Detection of Metastasis

The spread of cancer to distant organs, known as metastasis, is a major determinant of prognosis and treatment planning. Nuclear medicine provides highly sensitive whole-body imaging, making it an ideal tool for detecting metastatic disease. PET/CT is especially effective in identifying metastases in organs such as the lungs, liver, bones, and lymph nodes. In many cases, it can detect metastatic lesions that are not visible on conventional imaging, thereby altering the stage of disease and



influencing treatment decisions (Jadvar, 2016). Bone scintigraphy using technetium-99m is another important nuclear medicine technique for detecting skeletal metastases, particularly in cancers such as prostate and breast cancer. Similarly, specialized radiotracers have been developed for detecting metastases in specific tumor types, further enhancing diagnostic accuracy.

3.5 Role in Personalized Cancer Management

Nuclear medicine is increasingly contributing to the development of personalized cancer care. By providing detailed information about tumor biology, it helps clinicians tailor treatment strategies to individual patients. For instance, imaging of receptor expression using specific radiotracers can identify patients who are likely to benefit from targeted therapies. This approach not only improves treatment outcomes but also minimizes unnecessary exposure to ineffective treatments (Baum & Kulkarni, 2012). Furthermore, nuclear imaging can be used to monitor disease progression over time, allowing for dynamic adjustment of treatment plans. This adaptability is particularly important in oncology, where tumor behavior can vary significantly between patients.

4. Therapeutic Applications Of Nuclear Medicine In Cancer

In addition to its diagnostic capabilities, nuclear medicine has established a significant role in the treatment of cancer through targeted radionuclide therapy (TRT). This therapeutic approach involves the delivery of cytotoxic radiation directly to tumor cells using radiopharmaceuticals, thereby minimizing damage to surrounding healthy tissues. Unlike conventional radiotherapy, which delivers external radiation, radionuclide therapy works from within the body, offering a more

selective and personalized treatment strategy (Dash et al., 2015). The effectiveness of nuclear medicine therapy is largely based on its ability to exploit specific biological characteristics of tumors, such as receptor expression, metabolic activity, and cellular transport mechanisms. These targeted approaches have opened new avenues in oncology, particularly for patients with advanced or metastatic disease.

4.1 Targeted Radionuclide Therapy (TRT): Mechanism of Action

Targeted radionuclide therapy operates through a multi-step process:

1. **Target Recognition and Binding:** The radiopharmaceutical is designed to bind selectively to tumor-associated targets such as receptors, antigens, or transport proteins. This ensures preferential accumulation in cancer cells.
2. **Cellular Internalization (in some cases):** After binding, certain radiopharmaceuticals are internalized into the cancer cell, enhancing the delivery of radiation directly to intracellular targets.
3. **Radiation Emission and DNA Damage:** The radionuclide emits ionizing radiation (alpha particles, beta particles, or Auger electrons), which interacts with cellular components, particularly DNA. This leads to:
 - Single- and double-strand DNA breaks
 - Generation of reactive oxygen species (ROS)
 - Disruption of cellular replication mechanisms
4. **Cell Death:** The accumulated damage ultimately results in apoptosis, necrosis, or mitotic cell death. Importantly, the “cross-fire

effect” allows radiation to affect neighboring tumor cells, even if they do not directly bind the radiopharmaceutical (Sgouros et al., 2020).

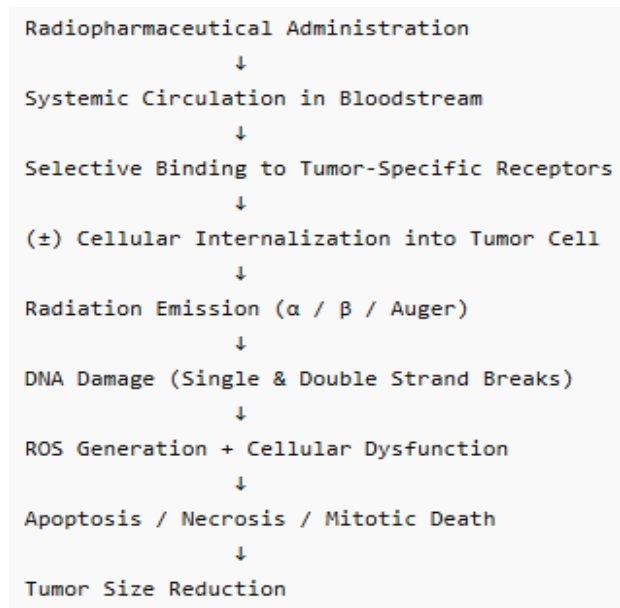


Figure 1: General Mechanism of Targeted Radionuclide Therapy (TRT)

4.2 Types of Radionuclide Emissions and Their Therapeutic Significance

The choice of radionuclide determines the type and range of radiation, which directly influences therapeutic outcomes:

- **Beta Emitters (e.g., Lutetium-177, Yttrium-90):** These particles have moderate tissue penetration (1–12 mm), making them suitable for treating medium to large tumors. They also contribute to the cross-fire effect, enhancing tumor coverage.
- **Alpha Emitters (e.g., Actinium-225, Radium-223):** Alpha particles have high energy but very short range (50–100 μm). This allows highly localized and potent tumor cell killing with minimal damage to surrounding tissues (Kratochwil et al., 2016).

- **Auger Electron Emitters:** These emit low-energy electrons with extremely short range, requiring close proximity to DNA for effectiveness. They are being explored for highly targeted intracellular therapies.

4.3 Clinically Established Radionuclide Therapies

4.3.1 Radioiodine Therapy (Iodine-131)

One of the earliest and most successful applications of nuclear medicine therapy is the use of iodine-131 in thyroid cancer. Thyroid cells naturally uptake iodine via the sodium-iodide symporter, allowing selective accumulation of radioactive iodine in both normal and malignant thyroid tissue.

Mechanism:

- Iodine-131 is actively transported into thyroid cells
- Emits beta radiation, causing localized cytotoxicity
- Leads to destruction of residual thyroid tissue and metastatic lesions

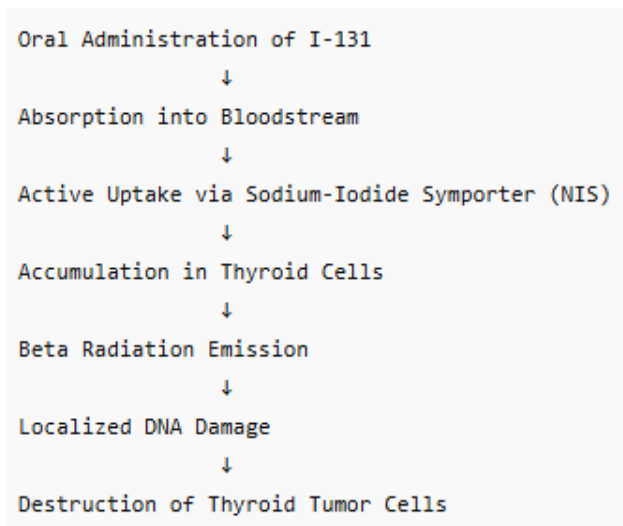


Figure 2 Mechanism of Radioiodine Therapy (I-131) – Thyroid Cancer

This therapy is widely used for differentiated thyroid cancer and has demonstrated excellent clinical outcomes (Schlumberger et al., 2012).

4.3.2 Peptide Receptor Radionuclide Therapy (PRRT)

PRRT is used primarily in neuroendocrine tumors (NETs) that overexpress somatostatin receptors.

Example: Lutetium-177 DOTATATE

Mechanism:

- Radiolabeled peptide binds to somatostatin receptors on tumor cells
- Internalization into the cell enhances radiation delivery
- Beta emission induces DNA damage and tumor cell death

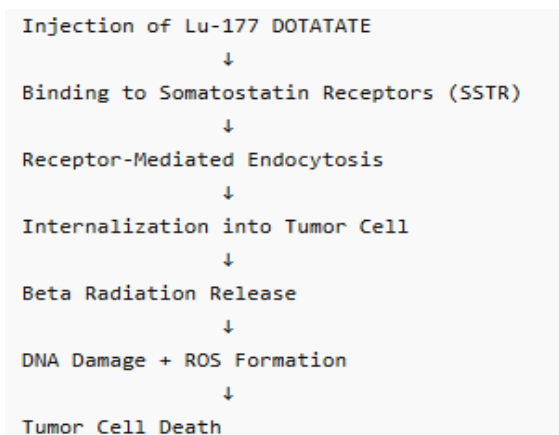


Figure 3: Mechanism of PRRT (Lutetium-177 DOTATATE)

PRRT has significantly improved progression-free survival in patients with advanced NETs (Strosberg et al., 2017).

4.3.3 Prostate-Specific Membrane Antigen (PSMA) Therapy

PSMA-targeted therapy is an emerging and highly promising approach for metastatic prostate cancer.

Example: Lutetium-177 PSMA

Mechanism:

- Radioligand binds to PSMA receptors overexpressed on prostate cancer cells
- Internalization leads to intracellular radiation exposure
- Induces targeted cytotoxicity with minimal systemic toxicity

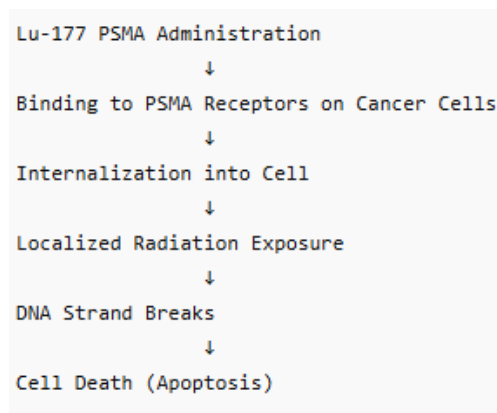


Figure 4: Mechanism of PSMA-Targeted Therapy (Prostate Cancer)

This approach represents a major advancement in precision oncology (Hofman et al., 2020).

4.3.4 Radioembolization (Yttrium-90 Microspheres)

Radioembolization is used for liver cancers, including hepatocellular carcinoma and metastatic liver disease.

Mechanism:

- Yttrium-90 microspheres are delivered via the hepatic artery
- Preferentially lodge in tumor vasculature
- Emit beta radiation, causing localized tumor necrosis

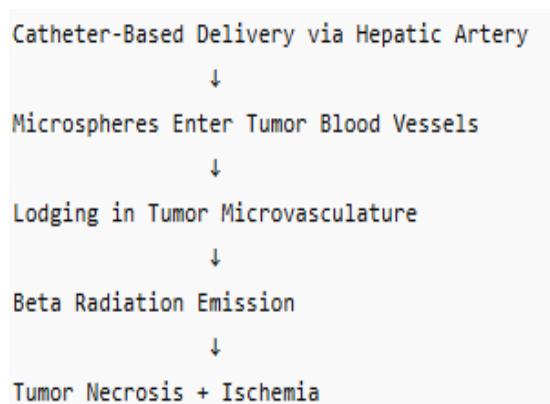


Figure 5: Mechanism of Radioembolization (Y-90 Microspheres)

This method combines embolization with radiation therapy, enhancing treatment efficacy (Salem & Thurston, 2006).

4.3.5 Alpha Therapy (Radium-223)

Radium-223 is used in metastatic prostate cancer with bone involvement.

Mechanism:

- Mimics calcium and selectively targets bone metastases
- Emits high-energy alpha particles
- Causes localized DNA damage in tumor cells within bone microenvironment

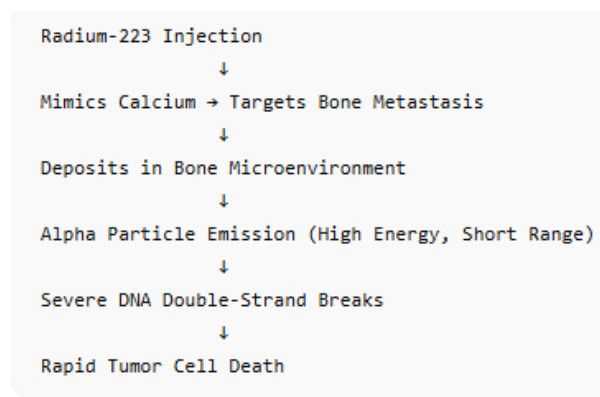


Figure 6 Mechanism of Alpha Therapy (Radium-223)

This therapy has been shown to improve survival and reduce skeletal-related events (Parker et al., 2013).

4.4 Theranostics: Integration of Diagnosis and Therapy

A major advancement in nuclear medicine is the concept of **theranostics**, where the same molecular target is used for both imaging and therapy. For example:

- Gallium-68 labeled compounds for diagnosis (PET imaging)
- Lutetium-177 labeled counterparts for therapy

This approach allows:

- Patient selection based on target expression
- Real-time monitoring of therapeutic response
- Personalized treatment planning

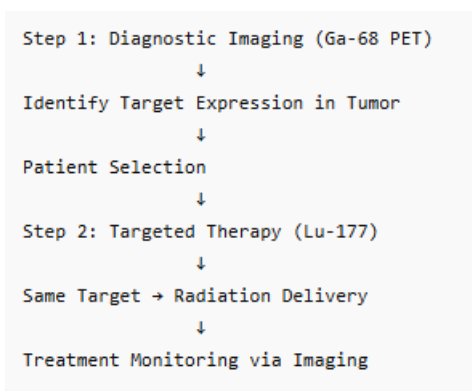


Figure 7: Theranostics Concept

Theranostics represents a shift toward precision medicine, ensuring that therapies are tailored to individual tumor biology (Baum & Kulkarni, 2012).

4.5 Advantages of Nuclear Medicine Therapy

- High specificity for tumor cells
- Minimal damage to normal tissues
- Ability to treat metastatic and inoperable cancers
- Potential for repeated administration
- Integration with diagnostic imaging (theranostics)

4.6 Limitations and Challenges

Despite its benefits, radionuclide therapy faces certain limitations:

- Limited availability of radionuclides
- High cost and infrastructure requirements
- Potential radiation toxicity (bone marrow, kidneys)
- Need for specialized facilities and trained personnel

Ongoing research is focused on improving targeting efficiency, reducing toxicity, and expanding clinical applications.

CONCLUSION

Nuclear medicine has fundamentally reshaped the landscape of oncology by enabling a shift from purely anatomical imaging to a more comprehensive molecular and functional approach. Through the use of targeted radiopharmaceuticals, it allows clinicians to visualize tumor biology, detect disease at an early stage, accurately stage malignancies, and monitor therapeutic response with high precision. This ability to assess cancer at the cellular level has significantly improved diagnostic accuracy and clinical decision-making. Beyond diagnosis, the evolution of targeted radionuclide therapy has opened new possibilities for treating a wide range of cancers, particularly those that are advanced or metastatic. By delivering cytotoxic radiation directly to tumor cells, these therapies achieve effective tumor control while minimizing damage to healthy tissues. The emergence of theranostics further strengthens this approach by integrating diagnosis and therapy into a single, patient-specific strategy, thereby advancing the principles of personalized medicine. Recent developments, including novel radiotracers, hybrid imaging systems, artificial intelligence integration, and nanotechnology-based delivery systems, continue to expand the scope and effectiveness of nuclear medicine in cancer care. These innovations not only enhance sensitivity and specificity but also contribute to safer and more efficient treatment modalities. Despite its considerable advantages, challenges such as high costs, limited availability of advanced infrastructure, regulatory complexities, and concerns regarding radiation exposure remain important considerations. Addressing these limitations through

technological innovation, improved accessibility, and standardized clinical protocols will be essential for broader implementation. In conclusion, nuclear medicine represents a powerful and evolving tool in the fight against cancer. Its unique ability to combine precise diagnosis with targeted therapy positions it at the forefront of modern oncology. With continued research and interdisciplinary collaboration, nuclear medicine is poised to play an increasingly central role in achieving more effective, personalized, and outcome-driven cancer care.

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