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Editorial

# Modulation Imaging Contrast Agent for Cancer

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**ABSTRACT**: Molecular imaging, also known as molecular imaging, is a medical technique used to visualize and analyze biological molecules in the human or animal body. According to the Society of Nuclear Medicine and Molecular Imaging's website, "Molecular Imaging" is a type of medical imaging that provides a detailed picture of what is happening in the body at the molecular and cellular levels. This definition refers to the significant advancements researchers have made over the past two decades in applying the principles of molecular imaging in various areas, from basic and translational science to advanced patient diagnosis and therapy. Essentially, molecular imaging allows us to visualize biochemical processes and target localization patterns that are invisible at the level of anatomical imaging. The goal of molecular imaging is to obtain information about molecular activity and function in living tissue. The technologies commonly used in imaging modulation are Positron Emission Tomography (PET), Single Photon Emission Computed Tomography (SPECT), and Magnetic Resonance Imaging (MRI).

**KEYWORDS**: Contrast agent; MRI; PET; Probes; SPECT

## 1. INTRODUCTION

Molecular imaging involves the use of radioactive compounds, contrast, or fluorophores that are injected into the patient's body. These compounds are designed to interact with specific targets in the body, such as receptors on the surface of cells, enzymes, or certain proteins (Lindner & Link, 2018; Sivasubramanian et al., 2022). When these compounds interact with these targets, they produce signals that can be detected and recorded by imaging devices (**Figure 1**).

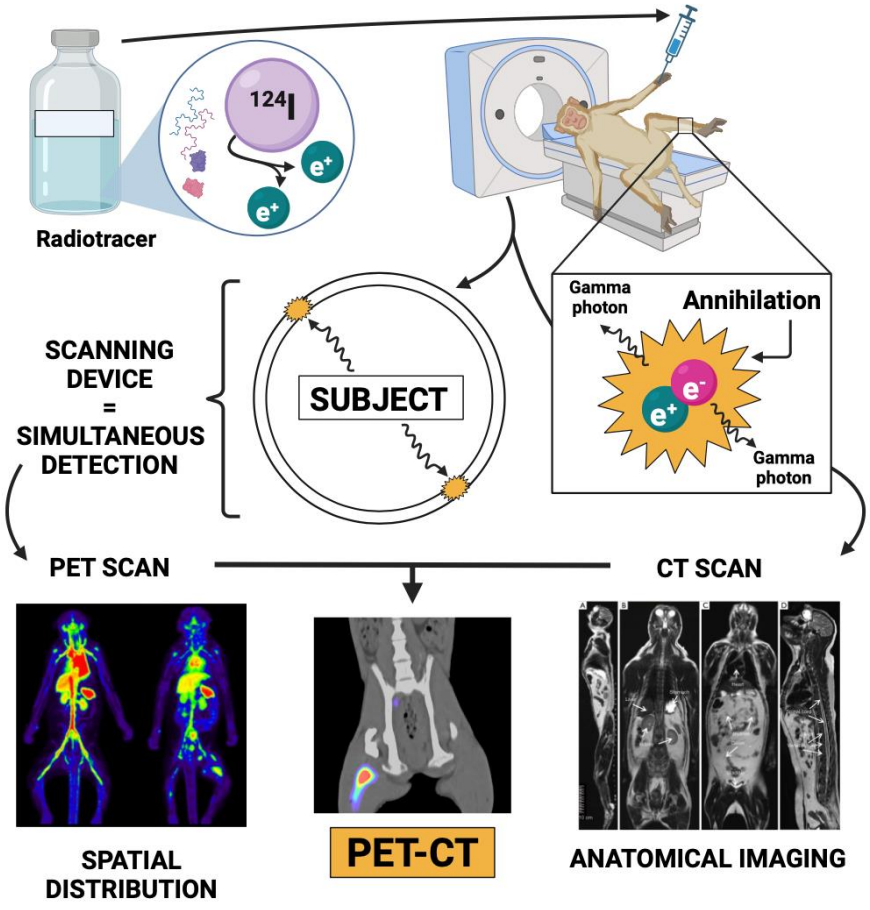


**Figure 1**. Use of radiotracer in experimental animals with PET/CT modulation (Created with Biorender.com)

## 2. RADIOPHARMACEUTICAL

Radioactive compounds in medicine are known as radiopharmaceuticals, which is a broader term that includes radiotracers and the pharmaceutical part of the compound. Radiopharmaceuticals consist of a radiotracer bound to a pharmaceutical portion that allows the administration and distribution of compounds into the body in a safe and effective manner (Dhoundiyal et al., 2024). Radiopharmaceutical can be carrier substances or drug molecules that are needed to direct the radiotracer to the desired target (Fawwaz et al., 2020). Radiopharmaceuticals may also include compounds designed to produce a therapeutic response in addition to diagnostic imaging (Crișan et al., 2022). For example, therapeutic radiopharmaceuticals are used in cancer treatment by utilizing radioactive isotopes to selectively destroy cancer cells. Efforts to develop radiopharmaceuticals are carried out through various stages as summarized in **Figure 2**.

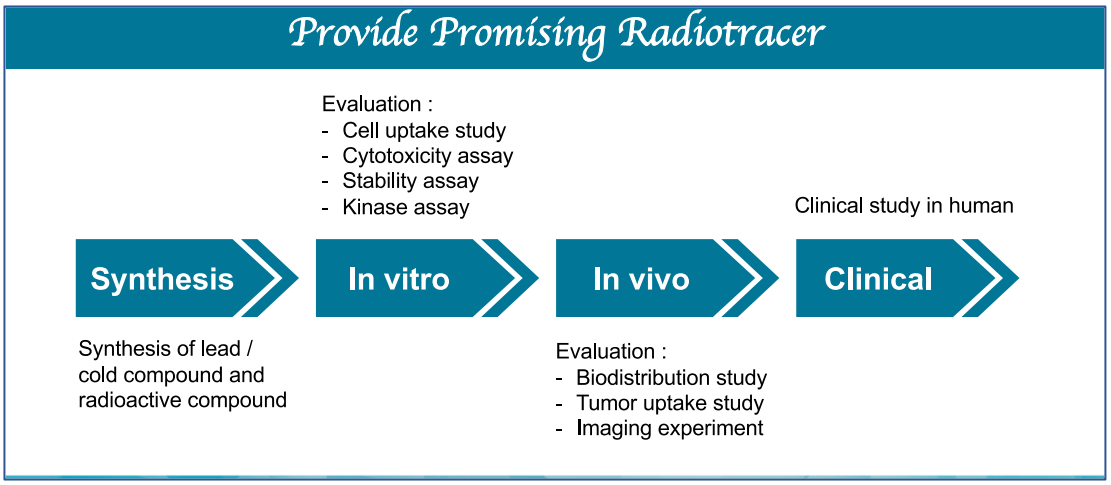


**Figure 2**. Flow of stages of development of radiopharmaceutical compounds

Radiotracers are chemical compounds containing radioactive isotopes attached to biological molecules or chemical compounds. These radioactive isotopes typically have short half-lives, meaning they undergo radioactive decay within a relatively short time after administration into the body (Crișan et al., 2022). Radiotracers emit radioactive signals that can be detected by imaging instruments, such as Positron Emission Tomography (PET), Single Photon Emission Computed Tomography (SPECT) (Ogawa et al., 2015; Valotassiou et al., 2012).

In practical applications, specially designed and manufactured radiopharmaceuticals are used in nuclear imaging procedures such as PET and SPECT. They are produced in customized radiopharmaceutical production facilities and are strictly regulated in terms of production, quality, and safety. Radiotracers provide important information about biological processes in the body and assist doctors in disease diagnosis, evaluation of response to therapy, and disease monitoring. They played an important role in the development of nuclear medicine and molecular imaging (Jødal et al., 2021).

## 3. MOLECULAR IMAGING MODALITIES

### 3.1. Positron Emission Tomography (PET)

PET is a molecular imaging technique that allows non-invasive detection of certain molecules and is expected to detect the presence of mutant EGFR. The diagnostic advantages of molecular imaging in cancer therapy can help in terms of early detection, staging, selection of therapy and planning and follow-up of therapy. PET is a non-invasive method that requires radionuclides that emit positrons (Rinne et al., 2021).

PET is a type of molecular imaging that can detect certain molecules non-invasively and is expected to detect the presence of mutant EGFR (Rinne et al., 2021). Molecular imaging has diagnostic advantages in cancer therapy, such as early detection, staging, selecting therapy, and planning and following up on therapy (Seaman et al., 2010). PET is a non-invasive method that uses radionuclides that emit positrons. PET uses a radiopharmaceutical that releases anti-electron particles (positron particles) which interact with electrons in the body. This interaction produces light emissions that can be detected and converted into a three-dimensional image. PET can provide information about organ function, such as brain glucose metabolism, and can also detect tumors and monitor the response to therapy (Zhu et al., 2011).

PET is a very promising method in molecular imaging. The basic principle of PET is that proton-rich radionuclides decay by emitting a positron ($\beta^+$), which then travels a short distance and decays with an electron ($\beta^-$) to produce two 511 KeV photons that appear almost exactly 180° apart. Detectors are used to detect the location of decay events. Common radionuclides used for PET imaging include organic/organic-like isotopes, such as carbon-11, nitrogen-13, and fluorine-18, and radiometals, such as gallium-68, copper-64, and zirconium-89. For many clinical and research applications, $^{18}F$ provides the ideal combination of drug chemical properties, radionuclide half-life ($T_{1/2}$ = 110 minutes), and positron yield and energy (Crișan et al., 2022; Rong et al., 2023).

Radionuclide-based imaging techniques such as PET play an important role in theranostics, which is a revolutionary approach that combines detection and therapy in patients. By changing the radionuclide in the chelator, such as $^{68}$Ga to $^{177}$Lu, or the halogen isotope, such as $^{123}$I to $^{I24}$I, one can switch from a diagnostic to a therapeutic agent in the same drug molecule simply by changing the radioisotope. The advantage of radionuclide-based theranostics is that it combines both detection and therapy in one drug molecule (Crișan et al., 2022; Gomes Marin et al., 2020; Rowe & Pomper, 2022).

### 3.2. Single Photon Emission Computed Tomography (SPECT)

SPECT is a molecular imaging technique that uses radionuclides to produce three-dimensional images showing the distribution of radiopharmaceuticals in the body (**Figure 3**). Radiotracers with single-photon-emitting radionuclides, such as iodine-123, indium-111, and technetium-99m, are commonly used in SPECT. The emitted photons of different energies can be differentiated by gamma cameras, enabling the simultaneous acquisition of multiple radiotracers. This makes SPECT useful for identifying heart defects, bone diseases, and neurological disorders (Crișan et al., 2022; Rinne et al., 2021).

Gamma cameras are used to detect the emitted photons from the nuclear decay process. These cameras consist of a scintillation crystal that converts the emitted photons into visible light, photomultiplier tubes that enhance the signal from the visible light, and a collimator that allows the emitted photons to be spatially localized. The collected data is then processed to produce three-dimensional images (Jarritt & Acton, 1996).

Although SPECT has limited resolution compared to other imaging modalities, it remains an important methodology in all areas of pathology that can be evaluated with imaging. SPECT is clinically ubiquitous, and radionuclides with long physical half-lives, such as indium-111, allow extended imaging for diagnostic purposes and dosimetry determination for certain therapeutic radiopharmaceuticals (Khalil et al., 2011; Salmanoglu et al., 2018).

In summary, although SPECT radiotracers lack the high resolution and routine quantification capabilities of PET radiotracers, the intrinsic advantages of radionuclides decaying with different energies and the wide range of available radiotracers will keep SPECT relevant for routine clinical applications in the future.

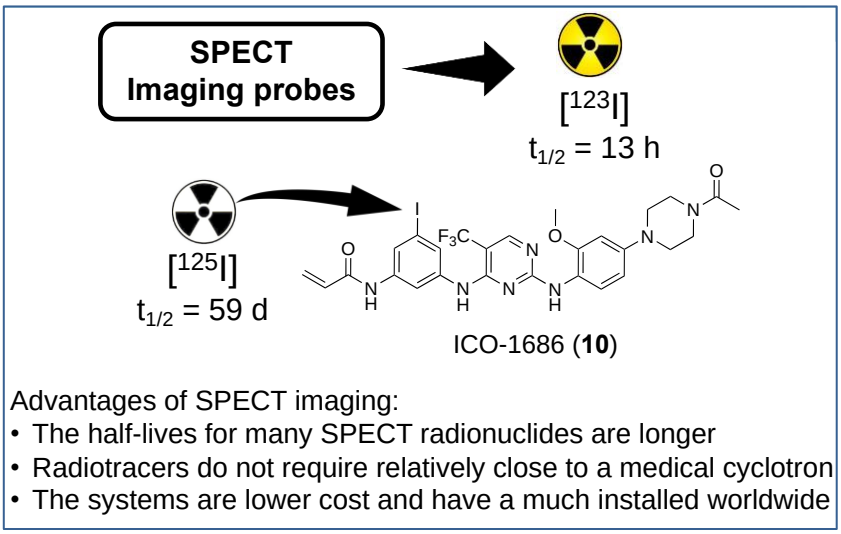


**Figure 3**. Radioisotope $^{123}$I used in the synthesis of the SPECT imaging probe

### 3.3. Magnetic Resonance Imaging (MRI)

MRI is a medical imaging technique that uses magnets and radio frequencies to create images of the body. While it's mainly used for anatomical imaging, there's also something called molecular MRI (Berger, 2002). This technique involves using a special contrast agent that interacts with specific molecules in the body. It can help diagnose and monitor diseases like cancer or heart disease (Petralia et al., 2021).

The basic principle of MRI is that atomic nuclei in the body can align like small magnets in a magnetic field. By applying radio frequencies, different signal patterns can be produced based on the composition of the tissue being imaged. This allows for high-resolution images of soft tissue structures like the brain and musculoskeletal system. MRI can also be used for molecular imaging, which involves identifying the resonances of protons and certain compounds. Magnetic Resonance Spectroscopy (MRS) can detect compounds that are present at high concentrations and have proton signals that can dissolve in water (Glunde et al., 2010; Glunde et al., 2011). Another technique called Chemical Exchange Saturation Transfer (CEST) can be used for compounds with lower concentrations (Grover et al., 2015).

Another use of MRI is imaging phagocytic cells in tumors and their metastases using Ultrasmall Iron Oxide Nanoparticles (USPIO) and other metal nanoparticles. Hyperpolarization MRI is another technique that aligns $^{13}C$-labeled agents to increase available signal. It can be used to investigate metabolic pathways in cancer (Li et al., 2023; Rahman, 2023).

## 4. CONCLUSION

Since the term was coined in the late 1990s, "Molecular Imaging" has developed rapidly as a field with tremendous potential to improve diagnosis and patient management. Molecular imaging continues to evolve with the discovery of new technologies and increased understanding of molecular biology. This allows researchers and medical professionals to gain deeper insight into biological processes in the human body, which in turn can aid in disease diagnosis, therapy monitoring, and the development of new drugs.

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