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Hybrid Imaging and Theranostics in Oncology

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Abstract

Advances in medical knowledge and better realizing disease processes are directing the search for early diagnosis/ imaging methods and new therapy choices.

Theranostics (or Theragnostic as it is a connection of Therapy and Diagnosis) is the combination of diagnostic imaging with targeted therapy and is, nowadays, becoming more widely applied. The study of theranostics combines molecular imaging with targeted radionuclide therapy, which involves the use of small molecules, peptides and/or antibodies as carriers for therapeutic radionuclides.

SPECT/CT and PET/CT hybrid studies are critical for use in medical conditions where isotopes detect life-threatening.

Greater quantities of radioisotope products in centers, around the world, are necessary.

There is also a shift towards reduced dependence on long-distance transport of radioisotope products. Clinicians increasingly seek to noninvasively inspection of tumour phenotypes and estimation of functional and molecular responses to therapy.

Keywords: Hybrid, Theranostics, Radiopharmaceuticals, Alpha- beta- particles, Cancer, Molecular Imaging

Abbreviations

- **FDA:** Food and Drags Administration
- **EMA:** European Medical Agency
- **LET:** Linear Energy Transfer
- **MoAbs:** Monoclonal Antibodies
- **NET:** Neuroendocrine Tumour
- **PCa:** Prostate Cancer
- **PRRT:** Peptide Receptor Radionuclide Therapy
- **PSMA:** Prostate Specific Membrane Antigene
- **RLT:** Radio- Ligand Therapies
- **RPT:** Radiopharmaceutical Therapy
- **SSTR:** Somatostatin Receptor

Introduction

Theranostics, the combination of diagnostic imaging with targeted therapy, is applied nowadays, widely.

The study of theranostics combines molecular imaging with targeted radionuclide therapy, which involves the use of small molecules, peptides and/or antibodies as carriers for therapeutic radionuclides. Radioactive isotopes are used in radioligand therapy to target cancer cells. Radioligand is a radioactive biochemical substance used for diagnosis or for research-oriented study. When radioligands attach to certain types of cancer cells in the body, there is a high possibility of obtaining the proper diagnosis or treatment. Radioactive medical isotopes, as specific medical isotopes applied in cancer therapeutics and effectively emit alpha α or beta β radiation, for very short periods, can destroy cancer cells inside tumours. For therapeutics, high Linear Energy Transfer (LET) radiations such as alpha (α), beta (β-) or Auger electrons are utilized to kill cancerous cells locally, while saving the normal tissues surrounding the malignant tumour cells.

Targeted α-Particle and β-Particle Therapy

α Particles have much greater mass, higher linear energy transfer (LET), travel a much shorter distance in tissue, and are more cytotoxic than β particles.

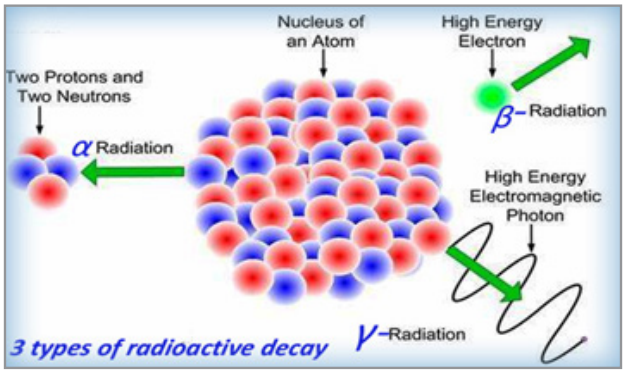

Figure 1: Radioactive decay by 3 types. The characteristic features of α and β particles are shown.

α Particles are positively charged particles composed of two protons and two neutrons (in spirit, the nucleus of a helium atom) and β particles are negatively charged particles, principally electrons.

α Particles have much greater mass, higher linear energy transfer (LET), travel a much shorter distance in tissue, and are more cytotoxic than β particles.

Gamma (γ-radiation) is a high energy electromagnetic photon that may be emitted by the radiopharmaceutical.

Schematically showed the characteristic features of α and β particles in Fig.1

α Particles are positively charged particles composed of two protons and two neutrons: as the nucleus of a helium atom, and β particles are negatively charged particles, the electrons.

β-emitters are radioactive nuclei that decay by emitting β- particle, which is an electron. During β-decay, a neutron within the nucleus is converted into a proton, which releases an electron and an antineutrino.

α -particles, as it is mentioned, have much greater mass, higher linear energy transfer (LET), that is, they move in a much shorter distance in tissue and are more cytotoxic than β particles.

Alpha- α -emitting radionuclides use in therapy are based on the short path length and high linear energy transfer (LET) of alpha radiation. Targeted alpha therapy guarantees a progress of cancer treatment.

For example, PSMA targeting vectors labelled with Actinium-225 (Ac225), have established the cancer therapy advancement using alpha- α- emitting radionuclides.

β-particles exert therapeutic effects through reactive oxygen species.

Gamma (γ-radiation) is a high energy electromagnetic photon that may be emitted by the radiopharmaceutical.

Auger Effect

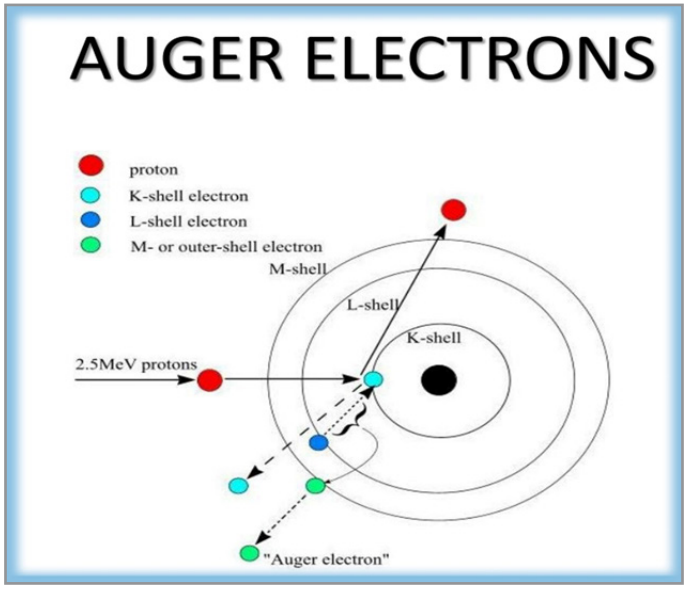

Figure 2: The diagram of Auger electron emission; the energy transferred to the outer electron to eject, it would not, in general, be transferred entirely to that electron but could also produce a photon alongside with the ejected electron.

If an inner shell electron is removed from an atom, an electron from a higher level will quickly make the transition downward to fill the vacancy. Sometimes this transition will be accompanied by an emitted photon whose quantum energy reaches the energy vacuum between the upper and lower level. For heavy atoms this quantum energy will be in the x-ray region; it is, generally, called x-ray fluorescence.

Alternatively, the energy released by the downward conversion, is transferred to one of the outer electrons instead of a photon. This electron is, then, ejected from the atom with an energy equal to the energy lost by the electron that made the downward transition; minus the binding energy of the electron, which is ejected, from the atom.

The analysis of the energy spectrum of these emitted electrons does give information about the atomic energy levels.

The Auger effect assumes closeness to internal conversion of the nucleus, which also ejects an electron. It is a process by which electrons with characteristic energies are ejected, from atoms, in response to a downward transition by another electron in the atom.

In Auger spectroscopy, the vacancy is produced, by bombardment, with high energy electrons; but the Auger effect can also occur if the vacancy is produced by other interactions. It is observed, as one of the methods of electron rearrangement, after an electron capture into the nucleus.

A high-speed electron knocks out an inner shell electron from an atom, leaving a vacancy. Sometimes an upper electron drops to fill the vacancy, emitting a photon; but sometimes the energy transferred, to an outer electron, ejecting it from the atom.

Theranostics, combines molecular imaging (hybrid studies by PET/CT or SPECT/CT) with targeted radionuclide therapy, typically with radionuclides that emit α, β or Auger radiation. Auger electrons are low energy electrons that are emitted, by radionuclides, that decay by electron capture as In111, Ga67, Tc99m, Pt195m, I125 and I123 [1]. This energy, is deposited, over micromillimeters distances, resulting in high linear energy transfer (LET) that is so strong to cause destructive damage in cancer cells. Auger Electrons, by therapeutic radioisotopic elements, have great capability for management of cancer.

Auger Electrons are most fatal to cancer cells when emitted near the cell nucleus and especially when incorporated into DNA. They can also kill targeted cancer cells by damaging the cell membrane and kill non-targeted cells through a cross-dose effect. This energy is deposited over nanometre-micrometre distances, resulting in high linear energy transfer (LET) that is effective in causing lethal damage in cancer cells.

Methods- Operation

Hybrid Imaging

SPECT/CT system: SPECT/CT has proven to be valuable in oncology. In the case of a patient, for example, with metastatic thyroid cancer, SPECT/CT, a hybrid image, precisely identifies where the doctor should operate. Combined SPECT/CT imaging provides sequentially functional information from SPECT and the anatomic information from CT, simultaneously. CT data are also used for rapid and optimal attenuation correction of the single photon emission data [2].

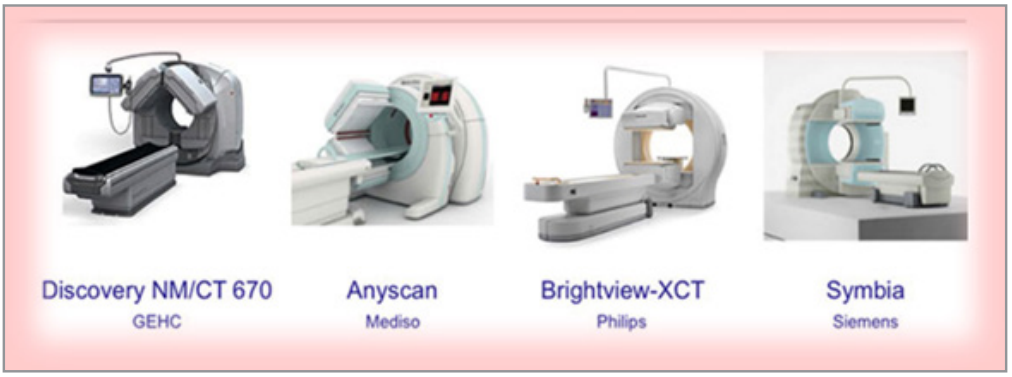

Figure 4: Selected state-of-the-art SPECT/CT systems. Since the introduction of the first commercial SPECT/CT system employing a dual-head SPECT and a low-dose, single-slice CT, SPECT/CT has advanced towards a hardware combination of multiple SPECT detector heads and spiral CT systems.

In Hybrid imaging: New tracers are spreading out the spectrum of clinical applications and innovative technological solutions.

Single photon emission computed tomography (SPECT) has enabled the evaluation of disease processes based on functional and metabolic information of organs and cells. Integration of X-ray computed tomography (CT) into SPECT has emerged as a brilliant diagnostic tool in medical imaging, where anatomical details may present functional and metabolic information [3].

The most important advantages of tomographic nuclear imaging techniques is the ability to accurately quantify the amount of radio-labelled biomolecules (radiotracers) in vivo.

PET/CT System

Patients with cancers of the head and neck, thyroid, breast, lung; cancer of unknown primary; lymphoma; and melanoma especially benefit from integrated FDG PET/CT.

A highly specific tracer is Ga68-DOTATOC, binds to somatotropin receptors, which are frequently overexpressed in neuroendocrine tumours. Because of their hormone activity, these tumours may be clinically important even when measuring less of 100 mg. Early detection is crucial; the localization of the primary, is required to show the detecting small tumour [4].

Figure 4: Images of commercially available hybrid imaging systems for clinical use. The figure shows three PET/CT systems. Images taken from vendor's web pages.

Development of new advanced imaging technologies allow for more specific and precise information, such as the use of faster Time of Flight (TOF) detectors, the design of total body systems with very high sensitivity, the introduction of organ-specific systems with very high spatial resolution and new probes for contrast-enhanced PET/CT. The concept of TOF assumes that the annihilation site of 2 photons originating from a single positron annihilation can be calculated from their travel time differences [5-7].

Hybrid imaging offer exclusive information on diseases that—when shared in larger-scale studies—can be applied in a "big data" approach to design automated, computer-based models for disease and therapy response estimate, both of which benefit also from ongoing technological and methodological improvements of hybrid imaging systems. The gains of hybrid imaging extend from diagnostic accuracy and faster examinations to interchange of know-how from different professional groups [8, 9].

Molecular Imaging- Radioisotope Production

Molecular imaging technologies are a crucial component of precision medicine-based advances to healthcare. Effective imaging tools detect diseases at an early stage of their expand, to evaluate prognosis and monitoring treatments for image-guided therapy.

Analysis of these high-content image data would assist physicians to diagnose better and treat diseases. SPECT/CT and PET/CT hybrid studies are critical for use in medical conditions where isotopes detect life-threatening [10].

The radioisotopes are produced in special nuclear reactors or generators, then transported to a production facility where the radioisotope is connecting to the cell targeting compound [11].

Therapy and imaging by Theranostics

Radiopharmaceuticals are not used only as therapy. Using a different radionuclide that is more suitable for imaging, they can be utilized to highlight if and where certain types of cancer exist in the body. Such drugs are used when performing positron emission tomography (PET) scans.

Example, the prostate-specific membrane antigen (PSMA) called Gallium 68 PSMA-11, that was approved for use December 2024, by the U.S. Food and Drug Administration (FDA). It is the first PET drug for imaging PSMA positive lesions in men with prostate cancer. Theranostics gives real-time information so that treatment may be altered based on an individual's cancer.

Radionuclides/ Theranostics

Therapeutic radiopharmaceuticals approved worldwide are used for the treatment of cancer. Radiopharmaceuticals are getting a raising attention, for cancer treatment, as they emit either α-rays or β-rays thus destroy the DNA of targeted tumour cells. To improve tumour uptake, novel targeted radionuclide-conjugated small molecules, peptides, and antibodies have been well developed, such as [I131] MIBG or [Lu177] Lu-DOTATATE [12].

Radionuclide	Therapeutic emission	Approximate emission range in tissue (mm)	Radionuclide half-life
Yttrium-90	β^-	5.30	64.1 hours
Iodine-131	β^-	0.8	8.0 days
Samarium-153	β^-	0.4	46.5 hours
Lutetium-177	β^-	0.62	6.6 days
Astatine-211	α	0.05	7.2 hours
Lead-212/bismuth-212	β^-/α	<0.1/0.05	10.6 hours/1.0 hours
Radium-223	α	0.05–0.08	11.4 days
Actinium-225	α	0.05–0.08	10.0 days
Thorium-227	α	0.05–0.08	18.7 days

Figure 5: Radionuclides in theranostics (from Sgouros et al 2020)

Ligands for Theranostics

Ligand is a molecule that is designed to bind to a target receptor or biomarker on cancer cells. This binding can be used to deliver a drug directly to cancer cells.

Radioligands attach to certain types of cancer cells in the body; then there is a high possibility obtain the proper diagnosis and treatment.

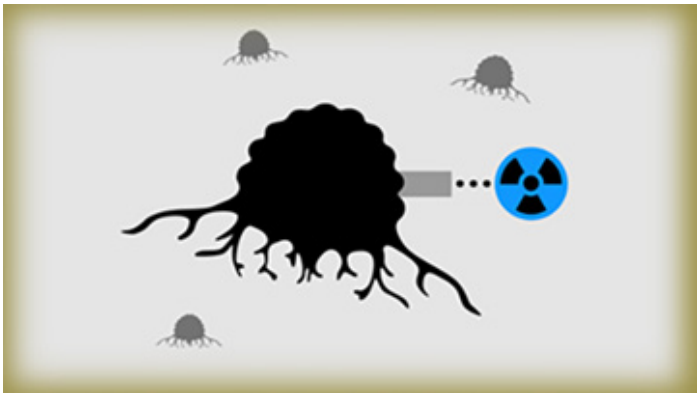

Figure 6: A radioligand is comprised of a radioisotope that binds the specific receptors or targets, allowing visualization and quantification of these cells.

A radionuclide held in a chelator is attached to a vector by a linker molecule. The vector binds to a molecular target or receptor to apply radiation to the target and obtain imagination for diagnostic and treatment purposes [13].

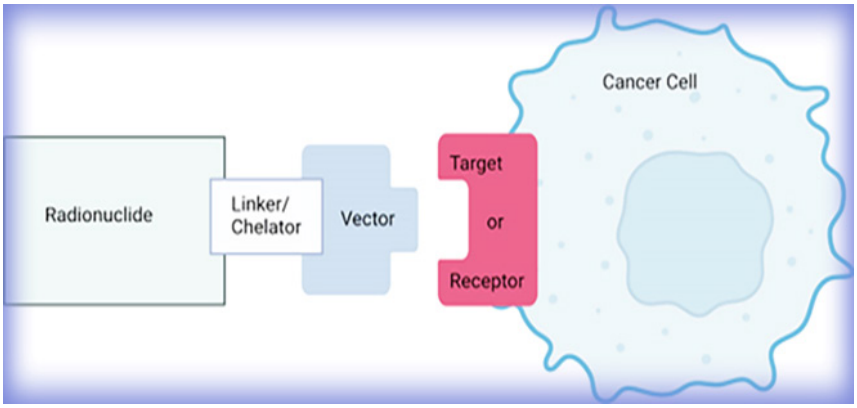

Figure 7: Radionuclide therapy schematic. A radionuclide held in a chelator is attached to a vector by a linker molecule. The vector binds to a molecular target to enable visualization of the target for diagnostic or treatment purposes and selective delivery of radiation therapy to the target. Alternatively, a free radionuclide ion can, in some circumstances, be used to target tumours or cancer cells, as with iodine 131, astatine 211, and radium 223.

How Theranostic Radiopharmaceuticals Work

/Designed to Take Radiation Directly to the Cancer/

Targeted therapies are designed to attach to specific receptors on cancer cells or non-malignant cells near a cancerous tumour. In targeted therapy work to kill cancer cells and stop a tumour from growing or spreading [13].

In targeted radiopharmaceutical therapy, a monoclonal antibody or other drug carries a radioactive isotope that will kill off cells—both cancer and healthy cells—in its immediate vicinity. Theranostics gives real-time information so that treatment may be altered based on an individual patient's cancer.

As, already referred, ligand is a molecule that is designed to bind to a target receptor or biomarker on cancer cells. This binding can be used to deliver a drug directly to cancer cells.

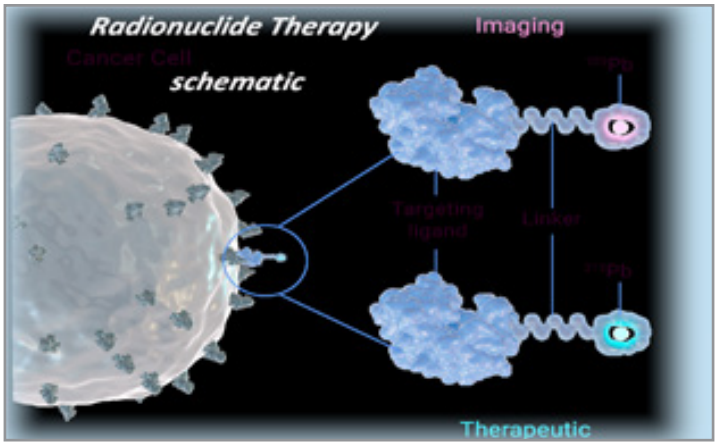

Figure 8: The radioligand molecule binds to a target receptor or biomarker on cancer cells to deliver a drug directly to cancer cells.

A radionuclide held in a chelator, is attached to a vector by a linker molecule. The vector binds to a molecular target to enable visualization of the target for diagnostic or treatment purposes and selective transfer of radiation therapy to the target.

When radioligands attach to certain types of cancer cells in the body, there is a high possibility of obtaining the proper diagnosis and treatment.

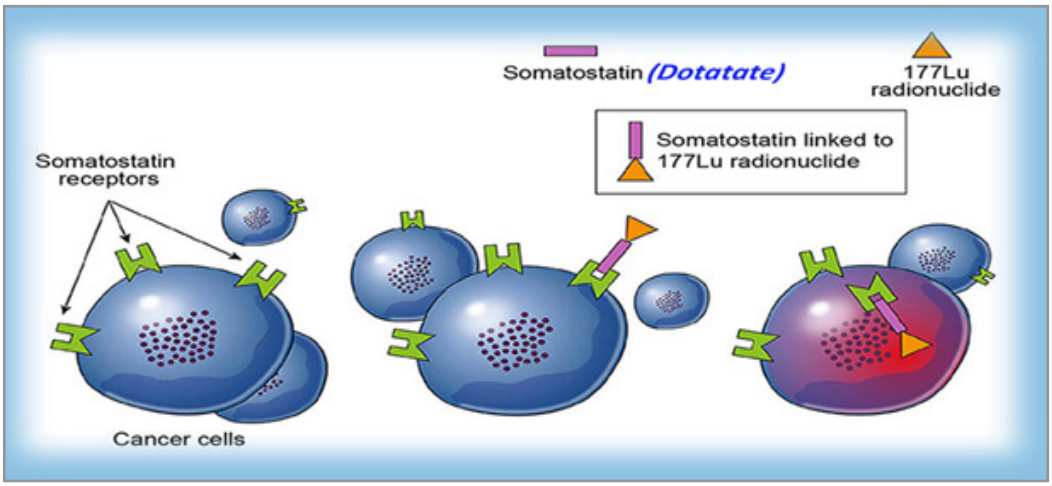

Figure 9: Lu177 can be imaged by SPECT/CT, Lu177 radionuclide linked to Somatostatin receptors in cancer cells.

Through chemical methods, a successful result can be obtained both, rapid clearance for Imaging and long-lasting tumour Therapy in a single molecule. The achievement of both rapid clearance for imaging and long-lasting tumour therapy in a single molecule is through chemical methods, which allows the accurate shift of a rapid excretion imaging agent to a long-acting therapeutic radio pharmaceutical. It can be accomplished by incorporating a chemistry-activated self-assembly or polymerization motif [14].

Discussion

Personalized cancer treatment obtained via Targeted Radionuclide Therapy (TRT) is of growing importance. Radionuclides with theranostic properties are proved to be clinically effective and widely used because diagnostic imaging and therapy are completed using a single preparation.

The radiopharmaceutical that can conduct diagnosis and therapy at the same time, thereby enhancing the suitability of theranostics and achieving the concept of "treating what you see." could be applied to multiple types of cancer [15].

During 2016 and 2018, the FDA successively approved [Ga68] Ga DOTA-TATE and [Lu177] Lu-DOTA-TATE for the diagnosis and treatment of well-differentiated neuroendocrine tumours (NETs) [16].

[Lu177] Lu-PSMA-617 was approved for the treatment of metastatic castration-resistant prostate cancer (mCRPC) in 2022, increasing the approval of theranostic method and suggesting directions for its future development. Among these isotopes, Lutetium-177 and Gallium-68 have been widely utilized radionuclides in recent years and have served as outstanding consorts for theranostics.

β-emitters

are the most used radioactive nuclides in clinical practice, are cytotoxic against large cancer deposits due to their emission of high-energy electrons in the medium tissue range (0.05–12 mm). The β-emission radionuclides approved by the FDA for use in radiotherapy include Yttrium-90, Lutetium-177, Iodine-131, and Strontium-89.

Lutetium-177 gains especial interest as the FDA approved:

- [Lu177] Lu-DOTATATE (Lutathera® commercial name) in 2018 and
- [Lu177] Lu-PSMA-617 in 2022 (Pluvicto commercial name).

The low energy β- particles emitted by Lu177 can efficiently target tumour tissues, while restricted in the surrounding normal tissues. These characteristics make Lu177 one of the most promising therapeutic radionuclides. [16]

However, the use of β-emitting radio nuclides has several limitations.

- β-emitters have, low energy and poor tissue penetration,
- resulting in lower treatment efficacy for larger and malignant tumours.
- α-emitters.
- α- emitting radioactive nuclei decay by emitting α particle,
- which consists of two protons and two neutrons.

α -emitting radionuclides are characterized of:

1. a shorter range of α- particles.
2. higher energy of emitted α-radiation.
3. irreversible damage to DNA caused by α radiation.

The clinical approval of [Ra223] RaCl2 (Xofigo) characterizes a point in the development and application of α- radiopharmaceuticals.

Though, therapeutic advantages of α nuclides have also, other α-emitters, such as: Actinium225, Astatine211, Thorium227

From a series of radioisotopes (α -emitters radiopharmaceuticals)
225Ac, 211At, 212Bi, 213Bi, 223Ra, 149Tb, 227Th, and 212Pb α-nuclides portrayals:

- The high-mass; pure α-emission radionuclides that can be used for targeted therapies have high production costs and a limited production ability, which restricts many systematic experiments.
- Improvement of the labelling methods, as the development of more efficient chelators is necessary, to strengthen the labelling stability more.
- A quantification method is needed to conduct extensive research on the dosimetric method and algorithm.

Radium-223

[Ra223] RaCl2, approved by the FDA for treating bone metastases from prostate cancer in 2013. It is the first accepted radiopharmaceutical that emits α-radiation. The natural characteristics of α-particles, as their short range and high energy, can cause permanent damage to the DNA of cancer cells. So, the expansion of novel α-particle targeted therapies is, at present, a powerful research topic.

Except for [Ra223] RaCl2, the other therapeutic radiopharmaceuticals are β-particle- radiopharmaceuticals that cause permanent DNA double-strand breakage in cancer cells. Phosphorus-32, Samarium-153, Strontium-89.

In addition to [Ra223] RaCl2, another three radiopharmaceuticals used for treating bone metastases are Sodium orthophosphate, [Sm153] Lexidronam, and [Sr89] SrCl2 [16].

Like Radium-223, these radiopharmaceuticals are calcium mimics that are examined in the skeleton as a component of the hydroxyapatite crystal together with calcium and the hydroxyl fraction.

Auger Electrons Emitters

Auger electron emitters are low-energy electrons produced by non-radiative transitions, and their range of action is much lower than that of α-particles and β-particles; thus, they can directly locate the lesion without damaging the surrounding cells.

These particles have a LET of 4-26keV/m and a tissue range smaller than the diameter of a single cell, making them ideal for nucleus targeting.

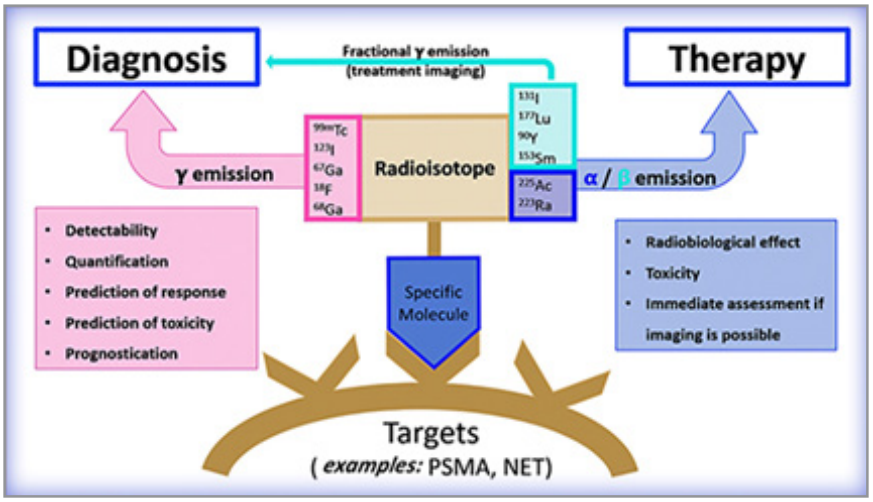

Figure 10: Radioisotopes emitting gamma γ-radiation (Tc99m, I123, Ga67, F18, Ga68), Alpha α- (Ac225, Ra223) At211, or Beta β-particles (I131, Lu177, Y90, Sm153) for Therapy are connected to specific molecules to targets. Gamma γ-radiation assists the quantification in the cancer image. Alpha and Beta particles function in radiobiological effect.

Through chemical methods, a successful result of both rapid clearance for Imaging and long-lasting tumour Therapy in a single molecule can be obtained. One approach to achieving both rapid clearance for imaging and long-lasting tumour therapy in a single molecule is through chemical methods, which allow for controlled shift of a rapid excretion imaging agent to a long-acting therapeutic radio pharmaceutical It allows for controlled shifting of a rapid excretion imaging agent to a long-acting therapeutic radiopharmaceutical and can accomplished by incorporating a chemistry-activated self-assembly or polymerization motif [17].

Personalized Treatment

Personalized cancer treatment obtained via Targeted Radionuclide Therapy (TRT) is of growing importance. Radionuclides with theranostic properties are clinically effective and widely used because diagnostic imaging and therapy can, in a single preparation, be completed [18].

In the procedure, either the same one radiopharmaceutical, which emits rays for diagnosis and particles for treatment, or two radiopharmaceuticals (one for diagnosis and the other for treatment) are used at the same time. Highly precise diagnostic and therapeutic radiopharmaceuticals can deal with specific tumours in the most effective manner [19].

The therapeutic effect of radiopharmaceuticals evolves biological effects of the radionuclides emitting radiation, resulting in DNA damage and targeted cell killing. A stand on potential mechanisms underlying radiopharmaceutical-induced cytotoxicity, including direct DNA cell death, ROS-mediated cell death and immunogenic cell death assists to understand the therapeutic mechanism of radiopharmaceuticals [20, 21].

Radiation Protection/Dosimetry

Radiation protection is of high concern in a production facility. There are regulations concerning the management of radiation. Instruments are required to measure the levels of radioactivity in a laboratory to ensure it is always restricted. We must indicate that the field of Radiopharmaceutical Therapy is expanding, and new standards and reliable applications should be produced.

Dosimetry

The dosimetry formalism requires a number of essential statements that do not apply for dosimetry calculations intended to assess potential toxicity or therapeutic efficacy.

In particular, the dosimetry scheme for risk evaluation does not incorporate tumour dosimetry because it relies on reference geometries.

The more direct approach of using the measured patient activity distribution from SPECT/CT or PET/CT images, overlaid over the anatomy as obtained by the CT portion of the imaging scan, can be determined.

Radionuclide treatments have the advantage to deliver lethal dose to cancer cells while keeping low dose to healthy tissue. Toxicity to the healthy tissue is the main problem during the radionuclide therapy. High absorbed dose to the kidneys may cause renal failure and high absorbed dose to bone marrow may cause myelotoxicity.

The accurate estimation of the absorbed dose to the tumour and the healthy tissue is essential for the efficiency of the treatment and the safety of the patient.

Voxelized dosimetry approaches use Monte Carlo or point- kernel methods to calculate maps of the spatial distribution of absorbed dose [22, 23].

These techniques make it possible to calculate the absorbed dose about actual patient anatomy, including tumours, rather than regarding a reference, population- averaged, geometry. Dosimetry studies have proved that great fluctuations occur in absorbed dose between patients that receive radionuclide therapy.

Dosimetry in radionuclide therapy often requires the calculation of average absorbed doses within and between spatial regions: for voxel-based dosimetry methods, for paired organs, or across multiple tumours. Formation of such averages can be made in different ways, starting from different definitions [23].

The Theranostic future- The Rise of Theranostics

Radiopharmaceuticals have transformed the disease diagnosis and treatment site, in oncology and they are used early in the treatment range.

Alpha-emitting isotopes like Actinium-225 (Ac-225) and Lead-212 (Pb-212) are to the guide of precision cancer treatment. Their potential to deliver high-energy doses directly to cancer cells, while sparing healthy tissue, is supreme [24].

Beta-emitting isotopes like Yttrium-90 (Y-90), Iodine-131 (I-131), Copper-67 (Cu-67), and Lutetium-177 (Lu-177) are playing an increasingly double role in the treatment of various cancers. Gallium-68 (Ga-68) have already demonstrated the effectiveness of this dual approach. These isotopes deliver beta radiation, which can effectively damage cancer cells [25].

Lu-177 has gained significant attention in current years due to its ability to treat neuroendocrine tumours and prostate cancer with targeted precision, other isotopes like Y-90 and I-131 remain dynamic mechanisms of treatments like radioembolization for liver cancer and targeted radiotherapy for thyroid cancer.

Cu-67 is emerging as a promising option for targeted therapies, with studies showing its potential in treating a range of cancers, including neuroblastomas and neuroendocrine tumours.

Copper-67 (67Cu) (t1/2 = 2.58 d), the longest-living radioisotope of Cu, is of supreme importance because of its simultaneous emissions of β− radiation
(mean β− energy: 141 keV; Eβ−max: 562 keV),
useful for therapeutic treatments
and γ-rays (93 and 185 keV),
suitable for single-photon emission computed tomography (SPECT) imaging.

In fact, the 67Cu mean β−-emission energy of 141 keV (Eβ−max: 562 keV) is slightly higher than that of Lutetium-177 (177Lu, β−-emission energy of 133.6 keV, Eβ−max: 497 keV).

67Cu decay characteristics make it one of the most promising theranostic radionuclides and its long half-life makes it suitable for imaging in vivo slow pharmacokinetics, such as monoclonal antibodies (MoAbs) or large molecules Theranostics continues to transform cancer care, combining diagnostic imaging with targeted treatment [26]. In 2025, we can expect further refinement of these technologies and expanded applications in oncology and beyond.

Conclusion

Theranostics, which combines diagnostic imaging with targeted therapy, represents a significant advancement in personalized oncology care. The integration of molecular imaging technologies, such as PET/CT and SPECT/CT, with therapeutic radionuclides enables precise cancer diagnosis and treatment. The use of α and β-emitting radiopharmaceuticals demonstrates potential for more effective and targeted cancer therapies while minimizing damage to surrounding healthy tissues. Continued developments in theranostic radionuclides and hybrid imaging systems are expected to further revolutionize cancer management and patient outcomes.

Guidelines

2022, European Journal of Nuclear Medicine and Molecular Imaging https://doi.org/10.1007/s00259-022-05785-x GUIDELINES Joint EANM, SNMMI and IAEA enabling guide: how to set up a theranostics centre, This enabling guide does not intend to answer all possible questions, but rather to serve as an overarching framework for multiple, more detailed future initiatives. It recognizes that there are regional differences in the specifics of regulation of radiation safety, but common elements of best practice valid globally.

2024, 07 October,1 EMA/CHMP/451705/2024 2 Committee for Medicinal Products for Human Use (CHMP) 3 Concept paper on clinical evaluation of therapeutic 4 radiopharmaceuticals in Oncology.

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