Original Article

Radiopharmaceutical Therapy: Its Therapeutic & Diagnostic Applications In Combating Cancer And Patents Thereof

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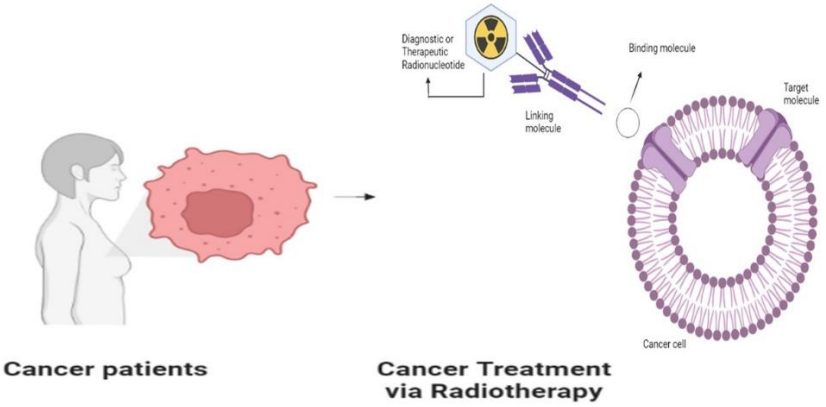
DOI: 10.47750/pnr.2023.14.S01.79



Abstract

Background: Radiopharmaceutical Therapy (Rpt) Offers Efficient And Secure Treatment For Many Cancer Types. These Therapies Ensure That The Targeted Tumour Receives A Concentrated Dosage While Maintaining The Surrounding Healthy Tissues.

Objective: Directly Attacking Malignant Cells While Safeguarding Healthy Tissues Is The Goal Of This Treatment. Rpt Offers The Benefit Of Sparing The Surrounding Healthy Tissues While Administering A Highly Concentrated Dosage To The Targeted Tumour Area.

Method: The Radioactive Elements Used In Radiopharmaceutical Treatment Kill Malignant Cells While Protecting Healthy Cells. All Of The Data In This Article Was Gathered After Research Was Done On Several Articles On Radiopharmaceutical Treatment For Cancer That Were Found On Sites Like Google Scholar And Pubmed.

Result: Radiopharmaceutical Therapy Is An Effective And Practical Choice Since It Has Less Toxicity Than Other Cancer Therapies. This Therapy Includes Radionuclides That May Be Used To Diagnose And Treat Cancer.

Conclusion: Radiopharmaceutical Treatment Is A Cutting-Edge Solution To The Cancer Problem. These Procedures Are Currently Among The Most Prevalent Cancer Treatment Options Because Of Their Minimally Invasive Nature And Shorter Treatment Times Than Chemotherapy.

Keyword: Radiopharmaceutical Therapy (RPT), Radionuclide, Prostate Cancer, Breast Cancer, Lung Cancer, Bladder Cancer, Ovarian Cancer, Pancreatic Cancer.

INTRODUCTION

Cancer is a broad category of illnesses that can affect nearly every organ or tissue in the body. When malignant cells multiply unrestrained and cross their usual boundaries to infect surrounding bodily parts or spread to other organs, these diseases are triggered. Cancer-related mortality is significantly impacted by the last step, known as metastasizing. The terms "neoplasm" and "malignant tumour" are also used to describe cancer. An estimated 9.6 million deaths, or one in every six deaths, were attributed to cancer in 2018, making it the second highest cause of death worldwide. Compared to

women, who are more likely to acquire cervical, breast, thyroid, colorectal, and lung cancers, men are more likely to develop liver, lung, prostate, colorectal, and stomach cancers [1]. Different forms of cancer are prevailing worldwide. It is known as a multifactorial disease. One of the causes of cancer is oxidative stress, which is the second leading cause worldwide, for many reasons pertaining to the expansion of the disease [2]. Radiopharmaceutical therapy aims to target cancer cells while safeguarding healthy organs directly. Sending radioactive substances with various emission characteristics into malignant tissue is known as radionuclide treatment (RT). The benefit of RT is that it protects the healthy tissues surrounding the tumour while providing a highly concentrated dose to the targeted tumour tissue. These procedures are currently one of the most prevalent cancer treatment options because they are minimally invasive and take less time to complete than chemotherapy [3].

Radioactive atoms are delivered to targets linked with tumours as part of radiopharmaceutical therapy (RPT). RPT is a cutting-edge therapeutic method that offers various benefits over currently used therapeutic modalities in cancer treatment. The radiation is provided systemically or locally, skin to chemotherapy, or biologically controlled therapy, rather than from outside the body, as is the case with radiotherapy. To enable a targeted therapeutic approach, cytotoxic radiation is delivered directly to cancer cells or their microenvironment or more frequently using delivery vehicles that bind specifically to endogenous targets or accumulate by various physiological mechanisms typical of neoplasia. It relies less on comprehending signalling pathways and finding drugs that block the proposed cancer phenotype-driving mechanism than biologic therapy (or ways). Notably, the failure rate of clinical trials for "targeted" (i.e., biologic) cancer medicines is 97% [4], which is partially attributable to the pharmaceuticals chosen for clinical trial research that target the incorrect pathway [5-6]. Radiopharmaceuticals are substances with radioactive isotopes (often referred to as radionuclides) that are used medicinally or in nanoceuticals. They can be either diagnostic or therapeutic, or both. Considering their radioactive characteristics, they form a distinct class of medications [7-8].

BIOLOGICAL AND PHYSICAL EFFECTIVENESS OF THERAPEUTIC RADIONUCLIDES

Understanding the type of ionising radiation that the radioisotopes in these compounds produce is the first step in establishing RPT. Ionizing radiation can come in three forms: photons, electrons, and alpha particles. X-rays and X-rays, which make up photons, have different energies; X-rays are less energetic. Photon emissions aid in the tracking of therapy responses following treatment; however, they are ineffective for pinpointing/identifying the location of lethal radiation in tumour cells [6]. Therefore, electrons and alpha particles are the recommended ionising radiation types for the therapy of tumour tissue. Beta particles have a long range and low linear energy, while alpha particles have the opposite characteristics [9]. For more than 50 years, radiopharmaceuticals have been employed in diagnostic and therapeutic procedures. RPT is less hazardous than several other cancer treatment options. Suitable radionuclide radiation type (alpha, beta, and Auger electron) selection, radiation energy higher than 1MeV, effective half-life in hours or days, high target tissue ratio/non-target tissue ratio, low cost, ease of procurement, and ease of preparation in the lab are some qualities of an ideal RPT. Because RPT is efficient, safe, and cost-effective, it has gained approval as a suitable treatment option for both primary and distant metastases [3, 6].

How to choose radionuclides for therapeutic purposes?

Ninety-five per cent of radiopharmaceuticals used in nuclear medicine are for diagnosis, and 5 per cent are for therapy. Diagnostic and therapeutic radionuclides are the two categories into which radionuclides fall, which are entitled as proactive molecules. 99mTc is the most popular and appropriate radionuclide for use in diagnostics. This radionuclide is preferred for use in diagnostics because it has isolated gamma rays with a force range of 100 to 250 keV, is readily accessible, inexpensive, sterile, pyrogenic, isotonic, and isohydric, has an efficient half-life, a high target/non-target ratio, and all of these properties. Other imaging radionuclides employed include gallium-68, carbon-11, nitrogen-13, oxygen-15, and fluorine-18. Thyroid cancer patients have received 131I therapy for over 50 years. In addition, the alpha (α) radionuclides 211As, 212Bismuth, 212lead, 213Bismuth, 225Actinium, 223Radium, and 227Thorium, as well as several beta radionuclides, such as 153Sm, 177Lu, Y-90, and 131I, are employed for therapeutic reasons. Table 1 below lists several therapeutic radionuclides' physical characteristics [3, 6, 9, 10].

Table 1: List of therapeutic radionuclides

Radionuclides	Mode of decay	Physical half-life ($t_{1/2}$)	E_{max} (MeV)
^{90}Y	Beta	64.10 hours	2.3
^{131}I	Beta	8.02 days	0.6
^{177}Lu	Beta	6.73 days	0.5
^{153}Sm	Beta	46.50 hours	0.8
^{186}Re	Beta, Electron capture (EC)	3.72 days	1.1
^{188}Re	Beta	17.00 hours	2.1
^{225}Ac	Alpha	10.00 days	5.8
^{213}Bi	Alpha , Beta	45.61 mins	5.9
^{212}Bi	Alpha, Beta	60.55 mins	6.1
^{211}At	Alpha, Electron capture (EC)	7.21 hours	5.9
^{212}Pb	Alpha, Beta	10.64 hours	0.6
^{223}Ra	Alpha	11.44 days	5.8
^{224}Ra	Alpha	3.63 days	5.7
^{227}Th	Alpha	18.68 days	6.0

HISTORY

After Henri Becquerel and Marie Curie discovered radioactivity in the early 1900s, radionuclide treatment began to gain popularity. After keeping a radium tube in his waistcoat pocket for several hours in 1901, Becquerel developed some acute skin irritation. Henri Alexandre Danlos and Eugene Bloch used radium for the first time in treatment when they applied it to a skin lesion caused by tuberculosis. Alexander Graham Bell proposed putting radium sources within or close to tumours in 1903, and Frederick Proescher presented the first research on radium intravenous injection treatment in 1913 [2]. Certain illnesses, such as systemic lupus, cancer, and nerve disorders, were treated using radium rays [11]. At the same time, radiopharmaceuticals containing particle-emitting radionuclides like strontium-89 chloride (Metatron), 90Y-ibritumomab tiuxetan (Zevalin), and iobenguane (131I-Azedra) were previously preferred in therapeutic radiopharmaceutical research. The 213Bi radionuclide received FDA (Food and Drug Administration) approval in 1997 to be used in clinical investigations. 223RaCl2 was the first radiopharmaceutical authorised by the US FDA in 2013 [3, 12].

CANCER

The term "cancer" is comprehensive. It explains the illness that develops due to unchecked cell growth and division by cellular alterations. While certain cancer types cause cells to grow and divide more slowly than others, some cancer types promote fast cell proliferation. While certain cancers, like leukaemia, may not cause visible growths known as tumours, others, like carcinoma, do. A cell is given the go-ahead to pass away so the body may swap it out for a younger, more functional cell. Cancerous cells are deficient in the elements that tell healthy cells to cease proliferating and to die. As a result, they accumulate throughout the body and consume nutrients and oxygen that would otherwise feed other cells. Tumours, immune system impairment, and other changes brought on by cancerous cells can prevent the body from operating normally. The lymph nodes may allow cancerous cells to spread from where they first appeared. Immune cell colonies may be seen all over the body [13].

Cancer can also be considered a functionally categorised step-by-step development with three phases: initiation, promotion, and progression [14]. Genomic alterations such as point mutations, gene deletion and amplification, and chromosomal rearrangements that result in irreversible cellular abnormalities define initiation inside the "cancer cell." The continued existence and clonal growth of these "initiated" cells aid in the formation of tumours. A significant increase in tumour size and either growth-related or mutually exclusive metastases are considered to be progression. The accumulation of genetic abnormalities in cells is crucial for cancer development. Such occurrences are undoubtedly necessary for the start of tumour formation, but they may also promote or advance it [14-15]. The primary abnormality in cancer formation is the quick, unpredictable spread of cancer cells. The overall result of a generalised loss of signal control for normal cell behaviour, which is represented by generalised growth control of the signal by many cell regulatory systems and is reflected in many aspects of cell behaviour that distinguish cancer cells from their regular counterparts, is that cancer cells multiply and divide uncontrollably, attack healthy tissues and organs, and eventually spread throughout the body [16]. The developmental stages of cells are shown diagrammatically in figure 1 below:

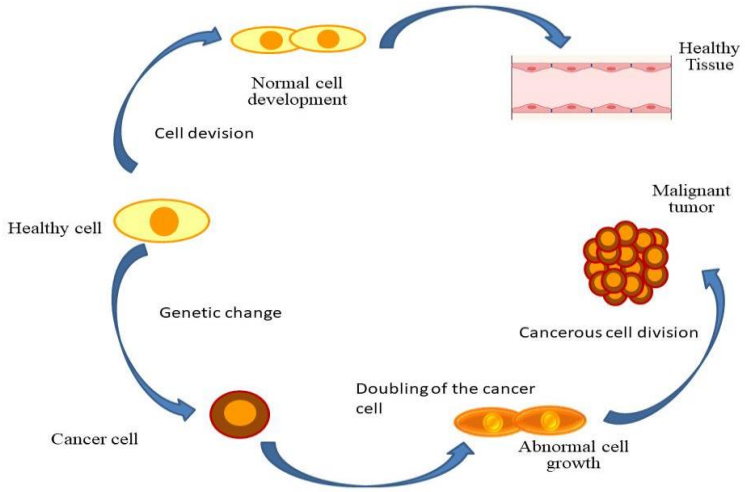


Fig.1. Developmental stages of cancerous cell and normal cell

TYPES OF CANCER

This list is an enlarged enumeration of the most specialised variants found within each main class; there are still over 200 types of tumours. The cancer names in quotation quotes are the shared names of some malignancies treated with radiopharmaceutical treatment; the list is incomplete [17].

- Breast cancer
- Bladder cancer
- Prostate cancer
- Pancreatic cancer

- Lung cancer
- Ovarian cancer

MECHANISM OF ACTION OF RADIOPHARMACEUTICAL THERAPY

RPT works by destroying cells through radiation-induced cell death. Soon after radiation and radioactivity were discovered, research into the effects of radioactivity on tissues and malignancies began. RPT benefits from utilising a good radiotherapy knowledge base [18]. Even though RPT is unique from radiation, it's crucial to comprehend how those aspects of RPT-specific therapy work [6]. A monoclonal antibody or other medication used in targeted radiopharmaceutical therapy contains a radioactive isotope that will destroy nearby cells, including cancer and healthy cells. In contrast to more conventional external beam radiation treatment (EBRT), which emits radiation from outside the body, this focused technique uses radiation from within the body [19].

Most radiopharmaceuticals are composed of a cell-targeting chemical and a tiny quantity of a radioactive substance (referred to as a radionuclide). Some radionuclides do not require combining or alteration since they can independently focus on particular cells or biological processes. When injected into the patient's circulation, the radiopharmaceutical travels to and delivers radiation to illness locations. Molecular therapy is referred to as a targeted therapy because it has a highly selective capacity to harm malignant cells while minimising radiation exposure to healthy tissue. Researchers are working on creating and testing novel radiopharmaceuticals in addition to the ones now being used to treat several malignancies, including advanced prostate cancer [20].

DIFFERENT TYPES OF CANCER IS TREATED BY RADIOPHARMACEUTICAL THERAPY

A. BREAST CANCER

Breast cancer is the second most common illness in middle-aged American women and the leading cause of cancer death in this population. The phrase "breast cancer" refers to cancers that originate in the breast tissue, most commonly in the lobules that supply the milk vessels with milk or the inner lining of the milk arteries. The second most common non-skin cancer form is breast cancer (behind lung carcinoma) and the 5th most frequent cause of malignant mortality worldwide, accounting for 10.4% of all cancer occurrences in women. Worldwide, breast cancer claimed 519,00 lives in 2004 (7 per cent of carcinoma deaths; almost 1 per cent of all deaths). Males typically have worse results owing to a delay in detection, although breast cancer affects women around 100 times more frequently than men. Cancer cells have comparable RNA and DNA to the organism's cells from whence they arose. The immune system does not often pick them up because of this [21]. Cancer can develop if the immune system is not functioning effectively or the number of cells created is too large for the immune system to remove [22]. The rate of DNA and RNA mutations may be high in some situations, such as those with an unfavourable environment (due to radiation, chemicals, etc.) [23], lousy diet (unhealthy cell environment) [24-25], people with mutation susceptibility genes [26], and seniors (above 80) [27-28]. Breast cancer, for example, refers to the uncontrollable development and multiplication of cells that begin in the mammary gland. Typically, cancer is named for the bodily area in which it began [29]. The glandulous and stromal tissues are the two basic tissue types that comprise the breast. The epithelial tissues contain the lobules, whereas the stromal tissues include the lipid and connective tissues of the breast and ducts that produce milk. The immune system's lymphatic tissue, which eliminates waste and cellular fluids, is also present in the breast [30]. Several tumour kinds can appear in various breast regions. Benign (non-cancerous) alterations cause the majority of breast tumours. For example, fibrocystic change is a non-carcinoma disorder that causes lumpiness in women, areas of thickening, discomfort, or breast pain, cysts (mount-up packets of liquid), and fibrosis [31]. Most breast tumours start in the duct-lining cells (ductal cancers). While a tiny percentage develops in other tissues, some (lobular cancers) begin with the lobule-lining cells [32-33]. For treating breast cancer, research into breast cancer therapy started in the 19th century. In 1937, radiation treatment was used in addition to surgery to protect the breast. Radiopharmaceuticals used to treat breast cancer are tabulated in Table 2, below:

Table 2. Radiopharmaceutical used in the treatment of breast cancer

S. No.	Radiopharmaceutical agent	Indication	Properties	Ref.
1.	^{188}Re-SOCTA-trastuzumab	Excessive amount of HER-2	overexpressing HER-2	[34]
2.	^{177}Lu-NT-AuNP	TNBC (triple-negative breast cancer) treatment		[35, 36]
3.	^{225}Ac®Fe3O4-CEPA-trastuzumab	Cancer cells have an accumulation of HER2 receptors.	breast cancer treatment	[37, 38]
4.	^{177}Lu-PSMA-617	PSMA	Specific targeting agent for TNBC (triple-negative breast cancer).	[39]
5.	^{111}In-AuNP-trastuzumab	Inhibit tumor growth	Breast cancer	[3, 40]

B. PROSTATE CANCER

The most commonly diagnosed male cancer, prostate cancer, is the fourth most common disease in men worldwide [41-42]. 1,414,249 new cases were identified in 2020, and this sickness caused 375,000 deaths globally [41-45]. Fortunately, most prostate tumours develop slowly, are low-grade, have a modest risk, and are not very aggressive [43]. Usually, there are no initial or early signs; however, there might be late symptoms, including fatigue brought on by anaemia, bone pain, paralysis brought on by spinal metastases, and renal failure from bilateral ureteral blockage [46]. When prostate cells experience DNA modifications, prostate cancer starts to spread. The instructions that inform a cell what to do are encoded in its DNA. The changes instruct the cells to multiply and develop at a faster rate than usual. When other cells would

perish, the aberrant cells would continue to exist. The abnormal cells build up into a tumour, which can spread to invade adjacent tissue. Over time, specific abnormal cells may separate and "metastasize" (apply to other areas of the body) [47]. Numerous instances of prostate cancer are found based on high plasmatic levels of PSA (> 4 ng/mL), a glycoprotein typically generated by prostate tissue. A tissue biopsy is the gold standard for determining the presence of cancer; however, men without cancer have been found to have elevated PSA levels. Diet and exercise significantly influence the onset and spread of prostate cancer [48-53]. Radiopharmaceuticals used to treat prostate cancer are tabulated in Table 3, below:

Table 3. Radiopharmaceutical used in the treatment of prostate cancer

S.no.	Radiopharmaceutical agent (radionuclide)	Company	Indication	Properties	Ref.
1.	^{227}Th- labeled PSMA- TTCa	Bayer	Prostate carcinoma	Emitter immunoconjugate that targets prostate cancer and PSMA	[54-56]
2.	^{177}Lu-PSMA-617	Endocyte/ Novartis	Prostate Carcinoma	binding mediated by PSMA	[57-64]
3.	^{177}Lu- labeled CTT-1403	Cancer Targeted Technologies	Prostate carcinoma	binding mediated by PSMA	[65-66]
4.	^{177}Lu- labeled PSMA-R2	Novartis/AAA	Prostate carcinoma	Internalization and binding are mediated by PSMA.	[67-69]

C. LUNG CANCER

Lung cancer is the world's worst malignancy [70], with the rate of lung malignancy continuing to increase, partly as a result of the diagnosis at a late stage, when therapies are less successful than they were at the beginning [71-72]. Although significant randomised studies have shown that high-risk people's mortality is reduced by lung cancer screening using chest low dose computed tomography (LDCT) [73-74], Fears about radiation exposure, potential harm from inaccurate imaging results, and potential morbidity from invasive diagnostic treatments, LDCT usage is still low, with just 6% of at-risk patients being tested [75-78]. Lung cancer can affect persons who have never smoked, although smokers are at a higher risk than nonsmokers. Smoking harms the lungs' lining cells, which leads to lung cancer. The lung tissue changes quickly after inhaling cigarette smoke, which is loaded with cancer-causing agents (carcinogens). Body might be able to repair this damage initially. However, the healthy cells lining lungs suffer increased harm with each subsequent encounter [79].

TYPE OF LUNG CANCER

Based on how lung cancer cells appear when examined under a microscope, there are two main forms of lung cancer. Depending on the primary form of lung cancer, it will decide how to proceed with therapy. The following are the two primary kinds of lung cancer:

- Carcinoma of the lung with few cells. Compared to non-small cell lung cancer, small cell lung cancer is less common and mainly affects heavy smokers.
- Carcinoma of the lungs is a non-small cell. Numerous lung cancers are referred to as "non-small cell lung cancer" in this context. Examples of non-small cell lung cancers include prominent cell carcinoma, adenocarcinoma, and squamous cell carcinoma [79]. Radiopharmaceuticals used to treat lung cancer are tabulated in Table 4 below:

Table 4. Radiopharmaceutical used in the treatment of lung cancer

S.no	Radiopharmaceutical agent (radionuclide)	Imaging Techniques	Indication	Properties	Ref.
1	^{18}F-FDG	Positron emission tomography (PET)	Somatostain receptor (SSTR) inhibition	Tumor imaging	[80-81]
2.	Re 188 P2045	Positron emission tomography (PET)	Somatostain receptor (SSTR) inhibition	Tumor imaging	[82]
3.	Tc 99m P2045	Positron emission tomography (PET)	suppression of SSTR	Tumor imaging	[83-84]

D. OVARIAN CANCER

The 7th most lethal illness for women and the 8th most often diagnosed tumour, ovarian cancer, accounts for roughly 185,000 fatalities per year globally [85]. The five-year relative survival rate for ovarian cancer is 93 per cent, and the 5-year cause-specific survival rates for endometrioid, mucinous, clear cell and serous ovary carcinoma are 82,71,66, and 43 per cent, respectively. Ovarian cancer is still among the most frequently diagnosed and aggressive urogenital female tumours. This is true even though screening methods have improved and anticancer surgical and pharmaceutical treatments have advanced [86-87]. 85–90% of all diagnosed ovarian tumours are epithelial, making up most of the ovarian cancer cases. On the other hand, germ cell ovarian cancers, which generally affect women between the ages of 55 and 65 and have an estimated onset of 20 years [88-89], account for 5% of all diagnosed tumours.

Types of ovarian cancer

- Ovarian epithelial carcinoma, which develops from the epithelium on the ovary's surface, is the most common. Primary peritoneal cancer and fallopian tube cancer fall under this category as well.
- Germ cell ovarian cancer is uncommon and originates from the reproductive cells of the ovaries.
- In contrast to stromal cell ovarian cancer, which grows from connective tissue cells.

• It is unclear whether the ovarian epithelial cells, sex-cord stromal cells, or germ cells are the source of the cells that make up the highly uncommon kind of ovarian cancer known as small cell carcinoma of the ovary. [90]. Radiopharmaceuticals used to treat ovarian cancer are tabulated in Table 5 below:

Table 5. Radiopharmaceutical used in the treatment of ovarian cancer

S.No.	AGENT	DRUG	Ref.
1.	Platinum-based therapies	Carboplatin	[91]
		Cisplatin	
		Paclitaxel	
2.	$PARP_1$	Niraparib	[91]
		Olaparib	
		Rucaparib	
3.	Non-platinum based therapies	PL Doxorubicin	[91]
		Abraxane	
		Pemetrexed	
		Topotecan	
4.	Antibody-drug conjugate	Anetumab	[91]
		Ravtansine	
5.	Anti-angiogenesis-based therapies	Bevacizumab + Paclitaxel	[91]
		Bevacizumab + PL Doxorubicin	
		Bevacizumab + Topotecan	
6.	Radiopharmaceutical	^{32}P phosphate	[91]
		^{227}Th conjugate	

E. BLADDER CANCER

Smoking, occupational exposure to carcinogens, aromatic amines, and urinary tract infections are the leading causes of bladder cancer. Based on data from atomic bomb survivors, the United Nations (UN) said in 2000 that there is "convincing evidence of a link between radiation exposure and bladder cancer risk" [92-97]. Research on persons who survived the atomic bomb typically produces risk estimates higher than those from most other studies. This could be because high-dose radiation kills cells rather than causing them to become cancerous [98-103].

A typical form of cancer that starts in the bladder's cells is bladder cancer. The cells (urothelial cells) that line the lining of the bladder are where bladder cancer most frequently develops. Ureters, which link kidneys to the bladder, contain urothelial cells. Although it can also occur in the kidneys and ureters, urothelial bladder carcinoma is significantly more prevalent. Most bladder cancer cases are discovered in their early stages when they are durable. However, even early-stage bladder tumours might reoccur following a curative regimen. Because of this, bladder cancer patients frequently require follow-up exams for years following treatment to check for bladder cancer that returns [104]. Brachytherapy, which involves implanting radium wires, has been used in radiotherapeutic methods to treat T1 tumours [105]. An energetic linear accelerator with a minimum of 4 MeV is needed to treat muscle-invasive illnesses known as external beam therapy effectively. Intravesical yttrium-90 in gelatin has been used as an unsealed source treatment [106]. Radiopharmaceuticals used to treat bladder cancer are tabulated in Table 6 below:

Table 6. Radiopharmaceutical used in the treatment of bladder cancer

S.no.	Radiopharmaceutical agent (radionuclide)	Half life ($t_{1/2}$)	Emitted radiation	Ref.
1.	Rhenium-188 (Re-188)	16.9 hours	β particle (maximal energy of 2.12 MeV)	[107-108]
2.	Copper-67 (Cu-67)	61.9 hours	β-emitting,distributed between 577 and 395 keV	[107, 109]

F. PANCREATIC CANCER

The pancreas is an organ in the abdomen that sits behind the bottom portion of the stomach. Pancreatic cancer starts in the tissues of the pancreas. The pancreas secretes digestive enzymes and produces hormones that control blood sugar. Being the tenth most common cause of death worldwide, pancreatic cancer is a substantial source of morbidity and mortality. Less than 5% of patients with ductal adenocarcinoma survive for at least five years overall [110]. The only known curative procedure is surgery [111-112].

Rarely is pancreatic cancer found in its earliest stages, when it is most treatable. This is since symptoms frequently don't appear until the disease has progressed to other organs. Many treatments for pancreatic cancer are available, depending on how advanced the illness is. Surgery, chemotherapy, radiation treatment, radiopharmaceutical therapy, or combinations of these are all possible options [113]. Radiopharmaceuticals used to treat pancreatic cancer are tabulated in Table 7 below:

Table 7. Radiopharmaceutical used in the treatment of pancreatic cancer

S.no	Radiopharmaceutical agent	Medical application	Properties	Ref.
1.	^{68}Ga-DOTA-NT-20.3	β therapy	ductal adenocarcinoma of the pancreas	[112,114]
2.	^{177}Lu (177Lu-3BP-227)	β therapy	Treatment for prostate cancer and metastatic pancreatic adenocarcinoma.	[112,115]
3.	^{177}Lu-DOTATOC	β therapy	cancer of the pancreas	[112,116]
4.	^{213}Bi-DOTATOC	β therapy	cancer of the pancreas	[112,116]

FUTURE PROSPECTIVE

Significant advancements have been achieved in the last ten years in the study and creation of pharmacological diagnostics and therapeutics for infections, inflammation, and disorders of the cardiovascular and central nervous systems, as well as cancer. Some radiopharmaceuticals have received commercial approval or are in the clinical translation phase. It has been recommended that radiopharmaceuticals be essential in enhancing the standard of living and access to healthcare via efforts made in the field [117]. Radiopharmaceuticals can be used in targeting various brain related diseases [118-120].

PATENTS

Various patents related to radiopharmaceuticals in cancer are tabulated in Table 8:

Table 8. Patents related to Radiopharmaceuticals use in cancer

Patent no.	Assignee/ Inventor	Filed on	Tittle	Methodology	Description	Ref.
WO2022081791A1	David L. Morse Thaddeus J. WADAS Darpan Pandya Narges TAFRESHI Mikalai BUDZEVICH	2022	Processes for synthesis of alpha-emitting radiopharmaceuticals	TLC NMR HPLC MS GC-MS (method of analysis)	It should be clear that the disclosures do not mean that changes and alternative embodiments are intended to fall within the scope of the specific embodiments and disclosed and that the invention is amenable to the claims' purview.	[121]
AU2018200419A1	Deutsches Krebsforschungszentrum DKFZ Universitaet Heidelberg	2018	Labeled inhibitors of prostate specific membrane antigen (PSMA), their use as imaging agents and pharmaceutical agents for the treatment of prostate cancer	PET - Imaging of MB17 Organ Distribution at 1 h Post infection. PET - Imaging of MB4. PET - Imaging of MB1 0	The current invention relates to radiopharmaceuticals and their use in nuclear medicine as tracers, imaging aids, and for treating various disease states associated with prostate cancer. The Glu-Urea-Lys (Glu NH-CO-NH-Lys) hydrophilic PSMA binding motif, a variable linker, and the chelator, ideally DOTA, make up the desired molecules of the present invention.	[122]
EP1521775B1	Immunomedics Inc	2015	Monoclonal antibody pam4 and its use for diagnosis and therapy of pancreatic cancer	"Affinity Enhancement System" (AES) Immunotherapy methods.	The term "PAM4 antibody" refers to murine and chimeric PAM4 antibodies. These antibodies might be a beneficial addition to the current PAM4 antibody immunodetection and immunotherapy techniques.	[123]
US7794691B2	EUROPEAN COMMUNITY REPRESENTED BY EUROPEAN COMMISSION European Community EC Belgium	2010	Radionuclides for medical use	Separation technique Positron emission tomography (PET).	Due to their decay properties (radiation, half-life), chemical stability under physiological settings, and capacity to bind to biological carrier molecules, these radionuclides are especially well suited for usage in humans and non-human species.	[124]

CURRENT CHALLENGES AND COST-EFFECT LIMITATIONS OF NEW RADIOPHARMACEUTICALS IN MARKET

The advantages of high sensitivity, selectivity, and favorable pharmacodynamics make radiolabeled compounds a promising candidates for diagnostics and possibly therapy. However, knowledge gaps in receptor expression patterns, receptor's higher order structures, and binding pattern on receptors need to be filled for full utilization of the approach. The radiolabeled compounds are promising candidates in diagnostics and can enhance the binding affinity and enable multi-targeting. There are many nanotechnology based radio-labelled theranostic systems are developed now a days, like liposomes, dendrimers, emulgels but owing to their price issue, they are not in reach of common man. On the scientific front, it has been recommended that nuclear medicine in combination with nanomedicine can provide a new way for diagnosing and treating cancer patients with lesser side effects [125-126].

CONCLUSION

In a highly effective way of treating cancer patients, intense short-range radiation is given systemically, which has several advantages over traditional therapeutic methods. RPT is an innovative approach used to treat a variety of tumours, including breast, prostate, bladder, and lung cancer. These procedures have been one of the most popular cancer treatment options in recent years due to their minimally invasive nature and shorter treatment times than chemotherapy. It is determined that the bulk of radiopharmaceuticals comprise a chemical that targets cells and a minimal amount of radioactive material (referred to as a radionuclide). Some radionuclides can focus on specific cells or biological processes on their own. Thus, they don't need to be combined or altered. The most frequently employed radionuclides in RPT therapy for cancer treatment are 131I and 177Lu.

DECLARATION

None

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

ETHICAL APPROVAL

Not applicable.

Consent to participate

Not applicable.

Consent to publication

Not applicable.

Availability of data and materials

Not applicable.

FUNDING

Not applicable.

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