Role of nuclear medicine in cancer therapy

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Abstract

Nuclear medicine is a multidisciplinary field that develops and uses instrumentation and tracers (radio pharmaceuticals) to study physiological processes and non-invasively diagnose, stage, and treat diseases. Particularly, it offers a unique means to study cancer biology in-vivo and to optimize cancer therapy for individual patients. A tracer is either a radio nuclide alone, such as iodine-131 or a radiolabel in a carrier molecule such as F-18 in fluoro deoxyglucose, or other feasible radio nuclide attached to a drug, a protein, or a peptide, which when introduced into the body, would accumulate in the tissue of interest. Nuclear medicine imaging, including single-photon emission computer tomography and positron emission tomography, can provide important quantitative and functional information about normal tissues or disease conditions, in contrast to conventional, anatomical imaging techniques such as ultra-sound, computed tomography, or magnetic resonance imaging. For treatment, tumor-targeting agents, conjugated with therapeutic radio nuclides, may be used to deposit lethal radiation at tumor sites. This review outlines the role of nuclear medicine in therapeutic treatment of cancer.

1 Introduction

Nuclear medicine therapy is a type of cancer treatment that involves the use of radioactive medicines that attach to cancer cells and kill them. Some persons with neuroendocrine tumours, prostate cancer, meningiomas, thyroid cancer, and lymphoma may benefit from this treatment. It has been shown to help with symptom relief, improved quality of life, and life extension. Nuclear medicine therapy is a type of cancer treatment that can be used

in conjunction with or after other treatments including chemotherapy and surgery. It probably won't heal you unless you mix it with other treatments. However, it will reduce symptoms and decrease and stabilise tumours in many patients, sometimes for years. For those who have failed to react to prior therapies, nuclear medicine therapy may be the best alternative.

The utilisation of radioactive substances as a medication is what makes nuclear medical therapy so successful (molecular radiotherapy). Tumor cells are recognised by the medication. It's administered intravenously, circulates throughout the body, adheres to tumour cells, provides radiation straight to them, and kills them. Some of the medicine never binds to cancer cells and floats around in the bloodstream until it is excreted, typically in the urine. The radioactive medicine eventually stops emitting radioactivity and ceases destroying cancer cells. To get the best results, nuclear medicine therapy is generally done several times.

Peptide receptor radio-nuclide therapy (PRRT), targeted radiation, radionuclide therapy, therapeutic nuclear medicine, and a theranostic approach to cancer treatment are all terms used to describe nuclear medicine therapy.

Radiopharmaceuticals that target particular tumours, such as thyroid cancer, lymphomas, or bone metastases, are used in nuclear medicine therapy to administer radiation to tumorous lesions as part of a therapeutic plan to cure, ameliorate, or manage the illness. It may be used to target specific areas or to cover the entire body.

Targeting the tumour :- Medical discoveries have resulted in a remarkable increase in the development and availability of novel cancer therapies. Chemotherapy, surgery, radiation therapy, and, more recently, targeted treatments, such as the use of radionuclide-based therapies in nuclear medicine, are all used in the treatment of cancer. External ionising radiation irradiation is the most often used radiation treatment for cancer patients. The main tumour and a small region surrounding it are irradiated with high-energy X-rays in this method.

Targeted radionuclide therapy, which involves delivering radioactive chemicals to patients, is another therapeutic option for certain forms of cancer. This medication, like chemotherapy, is a systemic treatment that travels through the circulation to reach cells all over the body. Unlike chemotherapy, however, these radioactive chemicals only target damaged cells, lowering the risk of unwanted effects.

Radiopharmaceuticals :- Radiopharmaceuticals with a high tumour affinity, also known as vehicles with a high tumour affinity, are best for therapeutic reasons. They can deliver precise dosages of radiation directly to tumours and their metastases, preserving healthy tissue in the process. The affinity – or binding power – of the molecule that delivers the radiation to the

tumour is determined by its affinity for the tumor's target structures, such as antigens or receptors. Ionizing radiation released by radionuclides coupled to the carrier damages cancer cells' DNA, causing tumours to shrink.

An ideal radiopharmaceutical for therapeutic purposes should:

- act exclusively in the cells of malignant tumours;
- reach all the cells of malignant tumours wherever they are localized;
- leave healthy tissues and organs unhurt while bringing maximum doses of radiation to the tumour;
- eliminate malignant tumour cells with great effectiveness.

How the therapy works :- The kind of ionising radiation released by the radionuclide determines the biological effect of a radiopharmaceutical. While imaging operations in nuclear medicine necessitate radionuclides that produce (gamma) radiation capable of penetrating the body, radionuclide treatment necessitates a separate class of radionuclides with optimal relative biological efficiency. The radionuclides most suited for tumour therapy are those that produce ionising radiation with brief tissue penetration, such as (alpha) or (beta) emitters, which release their energy near their targets.

2 Progression

2.1 Nuclear Medicine for Cancer Diagnosis and Treatment

Nuclear medicine may aid in the diagnosis and treatment of a variety of ailments, including cancer.

Doctors use nuclear medicine to inject small quantities of radioactive material into your body to assess how well your organs and tissues perform. This can assist them in detecting tumours and determining whether your cancer has migrated to other parts of your body. It can also aid in the targeting of cancer cells.

Nuclear medicine is also used by doctors to determine whether or not a therapy is effective.

2.2 How It Diagnoses Cancer

Nuclear medicine, like X-rays, is a kind of radiology. Nuclear imaging, on the other hand, displays the amount of activity in your organs and tissues, whereas X-rays provide specialists a "big picture" perspective of your anatomy.

When doctors employ nuclear medicine to diagnose or monitor an illness like cancer, they inject radionuclides (also known as "tracers") into your body that emit tiny doses of radiation.

Radionuclides can be taken orally or through an intravenous (IV) drip. You'll undergo a nuclear scan once you've taken these radionuclides. Scans are images of a specific part of your body that physicians use to discover cancers and other issues such as infection. A tumour, for example, may appear as a "hot spot" on the image, indicating that more radiation gathers in regions where the tumour is active. A tumour may sometimes appear as a "cool patch," indicating that there is less cell activity. This might potentially be a symptom of malignancy.

The sort of scan you receive is determined by your doctor's needs. The following are some of the most popular types of scans used to detect and monitor cancer:

Bone scans : These tests seek for cancer that has spread from other parts of your body to your bones. In rare cases, nuclear medicine can detect symptoms of bone cancer before X-rays can.

Gallium scans: Through an IV, a radioactive material called gallium is injected into your vein. It can assist your doctor in detecting cancer all throughout your body. Other issues, such as infection or inflammation, can be detected with gallium scans.

MUGA scans: Radionuclides are used by doctors to determine how well your heart pumps blood. This enables them to assess how effectively your heart functions prior to, during, and following specific forms of treatment. This is crucial because chemotherapy, especially in large doses, might impair how effectively your heart functions.

PET (positron emission tomography)scan : An IV infusion of radioactive sugar is given to you when you have this. Your physicians can use the quantity of sugar your cells ingest to figure out how fast your cancer cells are developing. PET scans are sometimes combined with computed tomography (CT) scans. These tests work together to assist doctors pinpoint the exact location of your malignancies.

Thyroid scans : You take radioactive iodine or get an injection to obtain one of them. Iodine accumulates in the thyroid gland, which aids doctors in the detection of thyroid cancer.

Nuclear medicine scans are non-invasive and painless. The scans normally include laying down on a table and having images taken by a doughnut-shaped scanning equipment. It normally takes 30 minutes to an hour to complete the process. Before your scan, you may need to refrain from eating or drinking for a period of time.

2.3 How Nuclear Medicine Treats Cancer

There are several types of nuclear medicine that treat cancer. They include:

Radioimmunotherapy : If your non-lymphoma Hodgkin's does not react to chemotherapy, your doctor may suggest this treatment, also known as RIT.

It combines radiation therapy with immunotherapy, a form of cancer treatment that relies on your body's immune system to fight the disease.

Monoclonal antibodies are given to you through an IV by a doctor. These are proteins created by humans that target specific areas of cancer cells. These antibodies are also tethered to a radioactive material.

These components work together to bind to cancer cells and send radiation straight to the tumour, killing it.

Radioactive iodine therapy : Almost percent of the iodine you consume is absorbed by your thyroid gland. Radioactive iodine (also known as RAI or I-131) gathers in thyroid cells during this therapy, destroying the gland and the cells.

Radioactive iodine (also known as radioiodine) treatment achieves this without harming the rest of your body, unlike certain other sources of radiation. Radioactive iodine is frequently used by doctors to eliminate thyroid tissue that surgery cannot remove. It may also aid in the eradication of thyroid cancer cells that have migrated to your lymph nodes or other places of your body.

Brachytherapy : To eliminate cancer cells, this method involves injecting large quantities of radioactive material into your bloodstream. In most circumstances, brachytherapy is more focused, has fewer side effects, and takes less time than traditional radiation treatment, which projects radiation into your cells using an external beam from outside your body.

Brachytherapy is sometimes used in conjunction with other cancer treatments, such as chemotherapy or surgery.

Y90 radioembolization: There are two stages to this liver cancer therapy. A catheter is inserted into the artery that provides blood to your liver in the first procedure. The other arteries that have anything to do with your liver are then "mapped out" by your doctor using a special dye. The radiation is introduced in the second stage. It's used to extremely small glass or

resin particles. The radiation is then directed into the hepatic artery after double-checking the location. The particles cling to the tumour and provide radiation to the tumour directly.

3 Imaging methods

There are three different functional imaging techniques under the general umbrella of nuclear medicine. The most Table 1 Examples of significant discoveries in nuclear medicine 1930s E.O. Lawrence developed the cyclotron at the UC Radiation Laboratory that later on produced the first medically useful radionuclides, including iodine-131, thallium-201, technetium-99 m, carbon-14, and gallium-67 1940s The first reactor-produced radionuclides for medical research were made at Oak Ridge National Laboratory (ORNL) including phosphorous-32, iron-52, and chromium-51 1950s Benedict Cassen invented the first automated scanner at the University of California at Los Angeles (UCLA) to image the thyroid gland after administering radioiodine to patients Hal Anger invented the stationary gamma camera (now known as the Anger camera) at the UC Radiation Laboratory The molybdenum-99/technetium-99 m generator was developed at Brookhaven National Laboratory (BNL) by Powell Richards 1960s Scientists at ORNL discovered the affinity of gallium-67 for soft-tissue tumors. This radionuclide had been used to image lymphomas, lung cancer, and brain tumors 1970s PET scanners were developed by Michael Phelps, Edward Hoffman, and Michel Ter-Pogossian at Washington University based on earlier work by Gordon Brownell at the Massachusetts Institute of Technology (MIT) and James Robertson at BNL 18F-FDG, a positron-emitting compound, was synthesized by chemists at BNL Scientists at the University of Pennsylvania and at the NIH used 18F-FDG to image glucose metabolism in the human brain 1980s A new radiopharmaceutical, iodine-131-m-iodine-benzyl-guanidine (I-131 MIBG), was developed by Donald Wieland for the diagnosis and treatment of rare childhood cancers Michael Welch of Washington University and John Katzenellenbogen of the University of Illinois developed the first PET radiotracer used to image tumors expressing the estrogen receptor 1990s A high-resolution PET scanner designed to image small laboratory animals (i.e., microPET) was developed at UCLA by Simon Cherry Radiolabeled antibodies were developed for therapy Advances were made in the application of alpha-particle emitters for therapy Tumor Biol. Author's personal copy basic is planar scintigraphy that provides information about the distribution of radioactive material in a single twodimensional image, analogues to a planar X-ray scan. As computer tomography presents three-dimensional

anatomical images, single photon emission computed tomography (SPECT) uses a series of contiguous two-dimensional images of the distribution of the radiotracer using the same agents as planar scintigraphy to provide a three-dimensional distribution of radiotracers. Finally, the most sensitive method, PET, utilizes -rays produced in the process of positron–electron annihilation and requires radionuclides emitting positrons. PET and SPECT have very high sensitivity as they allow detection of radiolabeled probe molecules in the 1011– 1012 and 1010–1011 range, respectively. This high sensitivity allows obtaining high-quality three-dimensional images, particularly useful for the detection and characterization of neoplasm. The noninvasive molecular imaging techniques complement well-established ex vivo assays, such as immunohistochemistry, fluorescence in situ hybridization, or enzymelinked immunosorbent assay, which require invasive sampling procedures and, because of tissue heterogeneity, may not always adequately represent the biochemical or pathological processes

4 Radionuclides

The radionuclide that is used is determined by the application. While radionuclides used in nuclear medicine imaging release -rays that may penetrate deep into the body, radionuclides used in treatment must emit radiation with a limited path length to deposit their energy locally and keep whole-body irradiation to a minimum. There are three of them kinds of particulate radiation with radioactive consequences beta particles, alpha particles, and Auger electrons are all used in treatment. The radionuclide's physical half-life should match the tagged monoclonal antibody's biological half-life (mAb), mAb fragments, tiny peptides, or small organic molecules are all examples of small organic molecules. To get the best SNR, you'll need a lot of molecules. In practise, the chosen isotope's half-life should be at least two times that of the event's biological half-life. To be imaged kinetics Its manufacturing should be done in a more efficient manner.

Simple and inexpensive. Furthermore, the chemical characteristics of radionuclides should make labelling easier and limit the accumulation of waste radiation in organs that aren't being targeted.

5 Radiotracers

Molecules that are small The radiolabeled glucose analogue fluorine-18-2-fluoro-2-deoxy-D-glucose (18F-FDG) is a fluorine-18-2-fluoro-2-deoxy-D-

glucose analogue. This nontumor-specific molecule that visualises glucose metabolism, which is commonly increased in tumour cells relative to normal cells, is by far the most extensively utilised nontumor-specific tracer for PET imaging (¿90 percent of all PET imaging procedures). Physiologic 18F-FDG uptake occurs in normal tissues because glucose metabolism is not particular to malignant processes (brain, muscles, salivary gland, myocardium, urinary tract). It's also taken up by a variety of inflammatory and benign lesions, which might result in false-positive or false-negative results.A great number of studies have shown that 18F-FDG imaging improves oncology staging and recurrence detection, and numerous outstanding publications evaluating the results have already been published. Analogue of thymidine with 18F labelling Nucleoside transporter proteins carry 3-deoxy-3-[18F]-fluorothymidine (18F-FLT) across cell membranes, where it is phosphorylated by thymidine kinase 1 (TK1), whose levels correlate with cell growth. The phosphorylated 18F-FLT is held intracellularly, similar to 18F-FDG, but it is not integrated into the DNA. 18F-FLT uptake in vivo has been shown to be a measure of tumour growth in a variety of cancers. Furthermore, 18F-FLT uptake is reliant on TK1 activity to activate a salvage mechanism that does not correlate with cell growth in all tumour types. Because the de novo route appears to be prominent in some cancer types, this lack of association might explain the differences in response between them.

6 Targeted radionuclide therapy

TRT (radioimmunotherapy) combines the benefits of radiation therapy with targeted immunotherapy utilising monoclonal antibodies (mAbs). The antibody is primarily used as a radiation delivery vehicle and has little effect on function. The therapeutic effect is produced through tissue absorption of the energy generated by the radionuclides tagged to mAbs in continuous, low-dose radiation. The kind of radionuclide utilised for RIT is determined by the nuclide's radiation properties, radiolabeling chemistry, and the type of tumour or cells targeted. Beta emitters are better suited for targeting bulky, solid tumours due to their lower energy and longer path length, whereas alpha emitters and Auger emitters are better suited for targeting single cells due to their high LET and short-distance energy deposition, as in micrometastatic disease, blood borne malignancies, and locoregional application. In clinical studies, RIT has been tested against a wide range of cancers. There are two different approaches that have been introduced into clinical practice including the use of direct conjugation of radioisotope tagged to mAb or pretargeting of the tumor. In the first case, the patient receives a diagnostic dose of an antibody labeled with a radionuclide compatible with an appropriate imaging

modality (SPECT or PET).

7 Future perspective

Modern oncology is moving in the direction of individualised medicine. The discovery and validation of new molecular targets for therapeutic intervention is ongoing. Regulatory agencies are encouraging the development of accurate prognostic and predictive biomarkers to be used in conjunction with new targeted medicines. Nuclear medicine imaging provides a unique noninvasive approach for in vivo characterization of tumour tissue, and it seems obvious that it will play a critical role in the future of oncology. The use of novel targeting molecules, improvement of radiolabeling methodology, and scanner technology advancements will improve the sensitivity and resolution of the pictures acquired. The clinical relevance of nuclear medicine will be enhanced further by the implementation of standard quality assurance processes that allow for accurate quantification of observable events.

Nuclear medicine is on its way to becoming a part of mainstream oncology, following the successful use of therapeutic radiopharmaceuticals for the treatment of malignant lymphoma. It is also a potential therapeutic method for the treatment of disseminated solid tumours, as evidenced by the success of a recent clinical study in patients with castration-resistant prostate cancer and bone metastases, as well as current preclinical research. The use of antibodies like trastuzumeb, pertuzumab, or cetuximab, which are being developed to interfere with cell signalling pathways, might be particularly promising in this area. These biological treatments, while initially beneficial in a small number of patients, quickly lose their efficacy as the targeted malignancies gain resistance. If the target molecules are still expressed in the tumour, the same antibodies might be employed to deliver therapeutic radionuclides to specific locations, extending their use. However, more work is needed to fully realise the potential of targeted radiation therapy, such as improving labelling methods, determining the best radionuclide or combination of radionuclides to treat specific tumour types, combining TRT with more traditional treatment modalities, and using new treatment planning strategies to properly adjust the administered dose of radiotherapeutics and the treatment schedule.

8 Conclusion

Nuclear medicine has a unique ability to improve cancer treatment outcomes by allowing doctors to personalise treatment for individual patients by determining tumour physiology and early response to therapy, as well as supplementing standard therapeutic approaches with targeted, systemic radiotherapy that can deliver cytotoxic radiation doses not only to the tumour bulk but also to spread metastatic disease, including undetectable micrometasts. Although the routine use of nuclear medicine in oncology is presently confined to 18F-FDG scans, a growing body of evidence suggests that it will be widely employed in the near future to aid cancer diagnosis, enhance therapy, and improve the success of therapeutic treatments.

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