

# NUCLEAR IMAGING: A TRENDY IMAGING MODALITY IN DENTISTRY

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## I. INTRODUCTION

The World Health Organization (WHO) recognizes Nuclear Medicine (NM) as an independent imaging technique, which involves the utilization of various radioactive substances for both diagnostic and therapeutic purposes in the field of medical research [1]. Nuclear medicine is a specialized field within medical science and imaging that employs radionuclides or radioisotopes, relying on the radioactive decay process for diagnosing and treating diseases [2]. This imaging technique not only evaluates physiological and biochemical changes but also aids in distinguishing between cells that are metabolically

inactive or deceased and those that are actively metabolizing. This capability allows for the detection of lesions before any morphological changes become apparent [3].

Nuclear medicine (NM) utilizes minimal quantities of radioactive substances, known as radiopharmaceuticals, for the purpose of disease diagnosis and treatment. These radiopharmaceuticals are typically administered to the patient through methods such as intravenous injection, ingestion, or inhalation. Radiopharmaceuticals, also referred to as radionuclides or radioisotopes, are unstable atoms of an element distinguished by varying neutron counts within their nuclei while maintaining the same number of protons and chemical properties. Their stability is quantified in terms of "half-lives [3]."

The full scope of nuclear medicine applications in dentistry remains to be fully comprehended. This chapter highlights the fundamental principles of diverse nuclear imaging techniques and their utilization in the examination of the oral and maxillofacial region. It underscores the importance of considering the diagnostic capabilities of nuclear medicine in oral and maxillofacial practice and aims to provide dentists with insights into various facets of this specialized imaging field to enhance the accuracy of diagnosis, treatment, and subsequent monitoring [4].

## II. HISTORY

Georg Charles de Hevesy, a Nobel Prize laureate in Chemistry, holds the distinction of being the pioneer in utilizing radioactive isotopes for investigating the metabolic processes in both plants and animals [7]. In 1925, Hermann Blumgart became the first to employ radioactive tracers in humans. He gauged the "circulation velocity" by monitoring the duration it took for radon-infused solutions to traverse from one arm to the other. To comprehend the dynamic behavior of the tracer, he conducted experiments involving the intramuscular injection of Bismuth-210 in rabbits. It is worth noting that De Hevesy is widely regarded as the founding figure in the field of nuclear medicine [Wagner HN][16].

The detection of artificial radioactivity in 1934, coupled with the production of radionuclides by Oak Ridge National Laboratory for medicinal purposes in 1946, marked significant milestones [2]. Nuclear medicine gained widespread recognition within the medical field during its golden era, which commenced in 1946 when Henkin RE et al. successfully treated thyroid cancer using radioiodine (I-131) [17].

Numerous radionuclides have been identified for medical applications, with Technetium-99 being the most extensively employed element in various nuclear medicine imaging procedures. Groundbreaking contributions from Benedict Cassen in designing the inaugural rectilinear scanner and the development of the scintillation camera (Anger camera) by Hal O. Anger expanded the emerging field of nuclear medicine into a fully established medical imaging discipline. Recent advancements in nuclear medicine encompass the introduction of positron emission tomography (PET), which has become an integral component of oncology for purposes such as diagnosis, staging, and treatment monitoring [2].

### III. DIFFERENT TYPES OF RADIO-NUCLIDE IMAGING

- Scintigraphy
- PET
- SPECT
- Fusion imaging
  - PET-CT
  - PET-MRI
  - SPECT-CT
- Lympho-scintigraphy

1. **Scintigraphy:** The Latin term "Scint" means "spark." A functional imaging method called bone scintigraphy can identify osteoblastic alterations with just a 10% deviation from the average [3].

Technetium-99m-methylene diphosphonate, or Tc-99m-MDP, is injected with 140 KeV gamma radiation to perform bone scintigraphy. Its physical half-life is brief, at 6 hours, and its affinity for hydroxyapatite can reach a high ratio of up to 40% [2]. Tc-99m-MDP attaches itself to the bone matrix through chemisorption. The basic idea is that, depending on the level of osteoblastic activity and the existence of vascularization, Tc-99m-MDP tends to accumulate in locations with high or active bone turnover [3, 7].

Diseases characterized by elevated metabolic activity, high synthesis of new bone, or enhanced turnover manifest as "hot spots," or regions of increased tracer uptake. "Cold spots" on bone scans are caused by inactive metabolic conditions, diminished or absent new bone production, or decreased vascular supply [5]. A computed scintillation camera is used in image acquisition to capture the gamma rays that the patient emits. When the gamma rays interact with the scintillation crystal in the camera, it fluoresces. Photomultiplier tubes, which convert light flashes into electronic impulses to create an image that is seen on a computer monitor, detect this fluorescence [4].

Bone scans encompass various techniques, including the Standard Bone Scan, 3-Phase Bone Scan, and Single Photon Emission Computed Tomography (SPECT). The Standard Bone Scan involves the acquisition of static images approximately 3 hours following the injection of a radiopharmaceutical. On the other hand, the 3-phase study comprises three stages: a flow assessment, a blood pool image, and the acquisition of delayed static views. The dynamic flow study necessitates the capture of rapid sequential images over a span of sixty seconds during the intravenous administration of the radiotracer. Subsequently, a blood pool image is obtained, reflecting tissue hyperemia and captured immediately after the flow study. It is important to note that three hours after the administration of the radiotracer, technetium-99m labeled diphosphonates exhibit maximal uptake in bone tissue, and a substantial portion of the unbound tracer would have been eliminated through renal excretion [11].

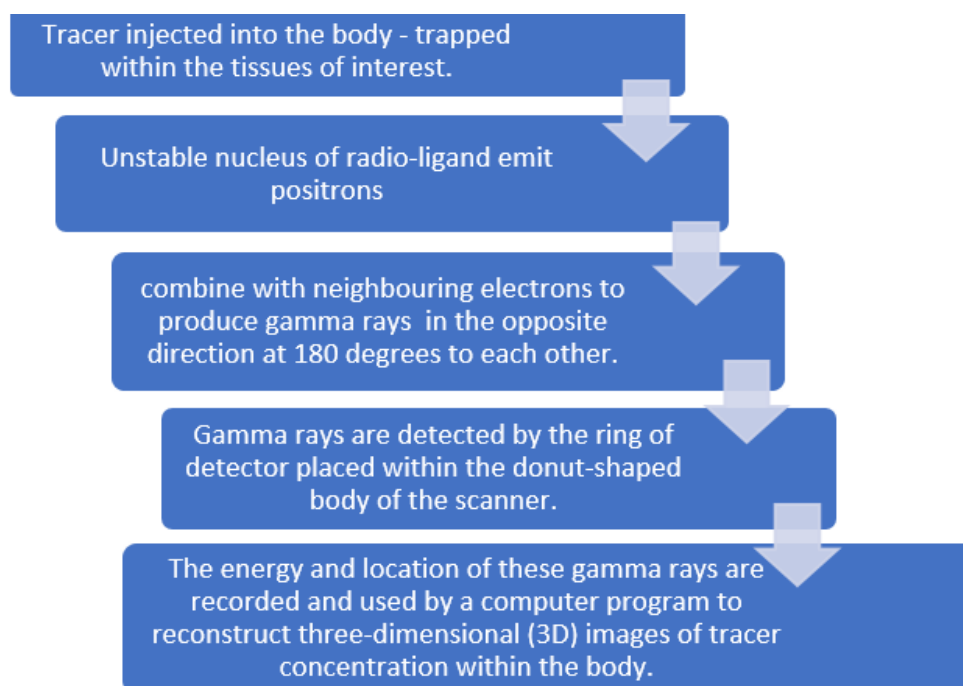
A rotating delayed static picture (usually sixty-four projections over 360°) is acquired for SPECT examinations. The images are then computer-reconstructed to provide three-dimensional multiplanar slices in the axial, coronal, and sagittal planes with respect to the patient's body [4]. Increased uptake on a bone scan will be indicative of any pathology

involving an osteoblastic response, such as inflammation, infection, primary or secondary malignancies, metabolic bone disease, or trauma [5].

### Indications of Scintigraphy

- Pre-operative evaluation of the malignant lesions.
  - Initial changes in the TMJ joint lead to joint disc abnormalities.
  - Salivary scintigraphy helps in measuring the fluid movement in acinar glands.
  - To assess the extent of bone activity in fibro-osseous lesions,
  - Inflammatory lesions of the jaws.
  - Cysts of the jaws.
  - Fractures.
2. **PET:**PET (Positron Emission Tomography) is a diagnostic imaging technique that identifies changes in metabolic processes within biological tissues. PET involves the utilization of tracers designed to interact with specific physiological mechanisms, such as glucose metabolism, facilitating the visualization and measurement of cellular functionality [1].

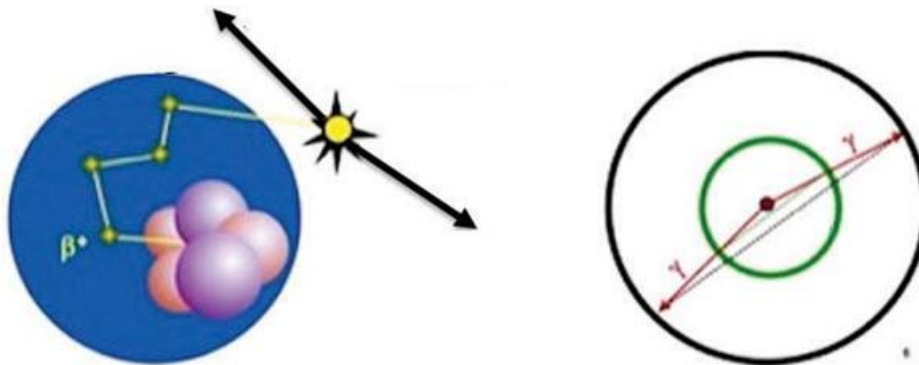
The increased need for improved imaging technologies is a result of the popularity of PET as a method for diagnosis, tumor and nodal staging, therapeutic prognosis monitoring, and recurrence evaluation in cancer [3].



**Figure 1:** Basic mechanism of PET

Within a PET scanner, there are multiple rings of detectors encircling the patient. Typically, these detectors employ crystals composed of bismuth germanate. These electronically connected, opposing detectors work in unison to simultaneously identify pairs of photons. They achieve this through coincidence detection circuits capable of measuring annihilation events occurring within a remarkably short timeframe

of 10-20 nanoseconds. The annihilation reaction transpires precisely along the line where two detectors meet. The initial PET scan data includes coincidence lines, which are subsequently recognized as projections. To generate a series of connected axial slices, this data undergoes processing using both back projection and iterative reconstruction algorithms. Subsequently, the PET computer reconstructs the transverse images from the projection data [6].



**Figure 2:** Annihilation Coincidence Detection (ACD)

Nuclear transition releases positrons, which scatter across matter while losing energy. They then annihilate with an electron to produce two photons that are emitted in opposite directions (left). It is presumed that annihilation happened on the line linking two encounters when they are recognized simultaneously (line of reaction, LOR). Through path analysis, ACD serves as a collimator for the positron emission tomography (PET) scanner, guiding the detected photons.

Frequently employed PET radioisotopes encompass  $^{11}\text{C}$ ,  $^{13}\text{N}$ ,  $^{15}\text{O}$ ,  $^{18}\text{F}$ ,  $^{64}\text{Cu}$ ,  $^{124}\text{I}$ , and  $^{89}\text{Zr}$ . These radioisotopes can be employed to tag various organic compounds (including glucose, amino acids, neurotransmitters, DNA nucleosides, antibodies, and more). This tagging enables the non-invasive practice of whole-body molecular imaging in the study of tumor biology [5].

The predominant clinical use of PET scans has involved the utilization of  $^{18}\text{F}$ -labeled fluoro-2-deoxyglucose ( $^{18}\text{F}$ -FDG). This radio-pharmaceutical, akin to glucose and possessing a half-life of 110 minutes, is primarily employed to investigate glucose metabolism in the brain and heart, as well as for identifying cancer metastases [6].

The Warburg effect, which states that cancerous cells ignore normal homeostatic control systems that govern growth and metabolism, provides the basis for the uptake of  $^{18}\text{F}$ -FDG. As a result, these cells consume a lot of glucose to fuel their development and hypermetabolism. These days,  $^{18}\text{F}$ -FDG PET/CT is a crucial diagnostic tool in oncology, especially for head and neck cancer (H&N) [5].

The semi-quantitative analysis of PET imaging uses the standardized uptake value (SUV), which is determined by dividing the injected activity in mega-becquerels by the body weight in grams and the mean ROI activity in mega-becquerels per milliliter [6].

- **Clinical Applications of PET**
  - Oral squamous cell carcinoma.
  - Identify pathology before a CT scan or MRI, at which point there are no palpable nodes in the neck.
  - PET scanning is an efficient method of determining the response to tumor treatment, recurrence, residual pathology, and distant metastases.

**3. Single-Photon Emission Computed Tomography [SPECT]:** employs gamma rays and, in terms of its capacity to deliver accurate three-dimensional data, is quite similar to a gamma camera. The majority of radiopharmaceuticals used in SPECT and nuclear medicine are tagged with photon-emitting radionuclides [1]. Unlike traditional Computed Tomography, which employs X-ray transmissions as the source of information, SPECT uses single photon gamma-ray emission. Similar to PET, SPECT uses gamma ray detection and radioactive tracer material. Whereas the tracers used in PET emit positrons that annihilate with electrons up to a few millimeters away, causing two gamma photons to be emitted in opposing directions at 180° to each other, SPECT tracers emit gamma radiation, which is directly measured[3].

The utility of Thallium 201 (<sup>201</sup>Tl) SPECT in the treatment of 18 patients with head and neck cancer was examined by Nagamachi et al. They found that while all primary tumors and cervical metastatic lymph nodes had increased uptake in both early and late images, there was no correlation between the tumor's size and histological type (Nagamachi et al. 1996 [13]).

**4. Fusion Imaging:** Fusion imaging, which is primarily responsible for improving diagnosis and formulating successful treatment outcomes, is the combination of several cutting-edge imaging modalities utilized in oral and maxillofacial imaging today [14].

- **Fusion Imaging Commonly Includes:**
  - Positron emission computed tomography (PET CT)
  - Positron emission tomography-magnetic resonance imaging (PET-MRI)
  - SPECT-CT
  - SPECT-CT with scintigraphy
- **Positron Emission Computed Tomography(PET-CT):** It was Dr. David Townsend, an imaging physicist at the University of Pittsburgh in 2000, who actually combined the two units into a single gantry. This minimizes the possibility of mis-registration and enables the simultaneous, instantaneous acquisition of the PET and CT data sets [14].

Through the use of hybrid PET/CT imaging, malignant tumors in the head and neck can be detected more accurately by better localizing metabolic anomalies and combining the functional information of PET with the anatomic data of CT. When used in the post-treatment context, PET/CT aids in distinguishing between inflammatory alterations following therapy and a recurring or residual tumor [6].

PET/CT has a high degree of sensitivity (>95%) when it comes to detecting cancer in the head and neck area. Using PET/CT, 77.8% with CT, and 85.2% with

MRI, the diagnosis performance was 96.3% for the primary tumors in the oral cavity. When MRI and PET scans were performed independently, the combined PET/MRI images demonstrated a greater sensitivity and specificity for the presence of cancer [1].

Because PET/CT-guided intensity-modulated radiation therapy (PET/CT-guided IMRT) can provide both anatomic and functional information, its application in tumor contouring, precise target volume delineation, and sparing normal tissues from radiation therapy has grown in importance [6].

❖ **Indications of PET/CT scan [7]:**

- To differentiate between benign from malignant lesions.
- Identify the unknown primary tumor if metastasis is the first tumor manifestation or if the para-neoplastic syndrome is present.
- Staging of a known tumor condition.
- Determine response to therapy in the case of known tumors.
- Assessing the presence of residual tumor disease.
- Determining recurrence, for example, with increasing tumor marker concentration.
- Selecting the exact site for biopsy.
- Help with radiotherapy planning and non-oncological issues.

❖ **Contraindications of PET –CT [7]:**

- Children below 2 years of age.
- Pregnant women.
- Persons over 60 years of age.
- Persons with complications after the previous administration of a contrast medium.
- Persons with acute and chronic circulatory and respiratory failure.
- Persons with hepatic and renal failure (also dialyzed patients).
- Persons with asthma and pulmonary edema.
- Persons with allergies.

❖ **Advantages of PET –CT scan**

- Provides anatomic and functional details, accurately.
- Less expensive.
- Less time-consuming.
- Provides minimum inconvenience to the patient.

❖ **Disadvantages of PET –CT scan**

- Pregnant women are unsuitable for a PET CT scan
- More radiation exposure.

- **Positron Emission Tomography-Magnetic Resonance Imaging (PET-MRI);** PET/MRI is a fusion imaging modality that combines PET functional imaging and MRI soft-tissue morphology imaging. When it comes to nodal staging, PET/MRI does not appear to be as helpful as PET/CT, but it does offer comparable N-staging accuracy when used as a whole-body staging strategy (Buchbender et al. 2012). [3].

In the early to mid-1990s, there were initial suggestions for integrating PET and MRI imaging devices into a single system (Hammer 1990, Hammer et al 1994). Strong magnetic field-detecting PET detectors (Shao et al., 1996) and prototype MRI-compatible PET scanners that could image small animals simultaneously with MRI began to surface shortly after (Christensen et al., 1995, Shao 1997). Human systems that can perform simultaneous (Delso et al. 2011) or sequential (Zaidi et al. 2011) PET and MRI acquisitions of the entire body are only commercially accessible after roughly 15 years of research [14].

❖ **Indications of PET –MRI [14]:**

- Soft tissue tumors
- In pediatric patients in turn reduction of radiation exposure
- TNM staging

❖ **Absolute contraindications of PET-MRI [14]:**

- The presence of implanted electrical and electronic devices represents a clear contraindication for magnetic resonance imaging (MRI), particularly including:
- Cardiac pacemakers (especially older models)
- Insulin pumps
- Implanted hearing aids
- Neuro-stimulators
- Intracranial metal clips
- Metallic bodies in the eye.

❖ **Advantages of PET-MRI**

- Better soft tissue contrast.
- Non-ionizing radiation.

The primary limitation of PET-CT is the high doses of ionizing radiation it exposes patients to. According to research, one PET-CT exposure is roughly equal to a one-year intake of

Interstellar radiation. In this regard, PET-MRI shows to be a superior imaging modality, offering morphological and functional features in a 30- to 60-minute examination that is quick, accurate, and thorough.

❖ **Disadvantages**

- Expensive.
- Diagnostic inaccuracy.

- **Single positron emission computed tomography (SPECT-CT):** SPECT, when combined with CT, allows for a direct correlation between anatomical and functional information, leading to improved localization and characterization of scintigraphy findings [1].

In 38 patients with head and neck melanoma, Vermeeren et al. calculated the added value of single photon emission computed tomography with CT (SPECT/CT)



for sentinel node detection and localization. They found that in 16% of the patients, SPECT/CT showed the anatomic location of the nodes clearly, and in all other patients, it showed an additional sentinel node [3].

The initial SPECT/CT system integrated a dual-head gamma camera and an attached X-ray transmission system on a single gantry. The CT image serves both for attenuation correction and anatomical imaging, and computer-assisted fusion of CT and SPECT images is utilized for display purposes [14].

❖ **Advantages;**

- Good image quality with high spatial resolution, contrast, and improved signal-to-noise image characteristics of SPECT.
- Determination of anatomy and extension of lesion.
- Accurate anatomic location of the lesion from CT.

❖ **Disadvantages:**

- Artifacts are more.
- Additional knowledge is required for accurate interpretation.

- **SPECT-CT with scintigraphy:** While software fusion has been investigated and shown promising results for co-registering SPECT with CT and MRI, it is not practical for everyday clinical use and takes a lot of effort. The literature is beginning to recognize that using SPECT/CT in conjunction with bone scintigraphy enhances diagnostic performance, mainly by improving specificity to more accurately differentiate between benign and malignant diseases. Combining the high sensitivity of SPECT with the high spatial resolution of CT, SPECT/CT is helpful in evaluating low back pain, bone infections, and long-term benign joint disorders in addition to postoperative consequences [14].

5. **Lymphoscintigraphy:** In lymphoscintigraphy, an appropriate radiopharmaceutical—typically technetium 99m—is injected through lymphatics to obtain tomographic and planar pictures. To locate and identify every sentinel lymph node (SLN) for surgical biopsy is the aim of lymphoscintigraphy. The main tumor's outflow initially reaches the SLN lymph node. If there are no indications of cancer in the SNL, the likelihood of the remaining lymph nodes being negative is also high. The prognosis is improved when only the SLNs are removed because there is no longer a need to remove any other lymph nodes, which also lessens any associated adverse effects [11].

Lymphoscintigraphy is demonstrating great potential in oral malignancies and serves as an intriguing scanning modality. The radioactive contrast is absorbed by lymphatic channels, leading to the initial draining lymphatic area known as the sentinel node, revealing the lymphatic spread pattern [9].

Lymphatic mapping can be effectively conducted using either radio-labeled tracers or vital blue dye (VBD). In conventional lymphoscintigraphy, the primary tracer employed is technetium 99m-labeled radio colloids. In the United States, the most commonly used radiotracer is technetium 99m-sulfur colloid, while in Europe, technetium 99m-albumin-based nano colloid is preferred. Both of these tracers exhibit suboptimal

rapid clearance from the injection site, significant accumulation in the initial node, and minimal tracer uptake in distant nodes [7].

#### **6. Advantages of nuclear medicine [3]:**

- Making the diagnosis prior to any morphologic alterations.
- Mostly provides images of function, such as biochemistry, metabolism, or physiology, by examining the dynamic behavior of molecules at various levels in organs and tissues.
- The interactive display makes it simple to demonstrate full body scans, which aids in the detection of metastatic activity.
- Detailed inspections can be carried out on various locations and at various periods following the injection of the tracer isotope to clarify results without exposing personnel to radiation repeatedly.

#### **7. Disadvantages of nuclear medicine [3]:**

- In general, the spatial resolution is not as good as that of other imaging modalities (CT/MRI).
- The machine that is being used is really expensive.
- Exam costs are also substantial and are influenced by the price of the radiopharmaceuticals that are utilized.
- When ionizing radiation is injected into their bodies, patients are exposed.
- Depending on the tracer's biodistribution and clearance kinetics, the patient's internal whole-body exposure to radionuclides is not uniform.
- While working with PET tracers, staff members are likely to be highly exposed to radiation.

### **IV. CONCLUSION**

nuclear examination Dentists should be conversant with the procedures that are frequently employed in nuclear medicine when it comes to oral lesions.

In order to evaluate the osteoblastic activity around implants and in periodontal disease, as well as to identify fractures, benign and metastatic tumors, bone grafts, and TMJ disorders at an early stage and help with intervention therapy, nuclear medicine imaging techniques have evolved into a routine diagnostic method. Bone scans, SPECT imaging, and PET scans are methods that aid in the diagnosis of cancers in the surrounding periodontal/oro-maxillary regions and oral/dental diseases. These tumors may initially need to be treated by dentists, but they may eventually need to be treated by oncologists. Due to its focus on function and use of imaging agents tailored to specific disease processes, nuclear medicine is a perfect specialization to adapt to the emerging field of molecular medicine.

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