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Review Article

Nuclear imaging in the field of dentistry: A review

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Abstract

Nuclear medicine(NM) imaging has played a vital role in the early diagnosis of disease in the recent decades. Although in the present time's conventional radiographs, Cone Beam Computed Tomography (CBCT), Computed Tomography (CT), and other alike imaging modalities are being routinely used for diagnosis and treatment purposes in the head and neck region, NM has been in use only for certain oral and maxillofacial pathologies. NM is an impressive and influential imaging means which relies on metabolic and other physiological processes of tissues revealing accurate functional and biochemical aspects of tissues and help in precise diagnosis. Radionuclide imaging involves the use radioactive isotopes that emit gamma (γ) rays. The γ rays thus emitted are detected by a gamma camera and different planar images are formed and shows the location of the radionuclides in the body. The technique provides an early marker of the disease after allowing the measurement of tissue function in vivo. Even though NM is not used on day to day basis in the field of dentistry, the dental professional must acquire the requisite information about its various uses. This review is an attempt at making a dental professional familiar with the functioning of NM imaging in the oral and maxillofacial region.

Keywords: Nuclear Medicine; Positron emission tomography(PET); Single photon emission computed tomography (SPECT); Fusion imagingi.

INTRODUCTION

Nuclear medicine (NM) belongs to a specialized field of imaging, involving radionuclides, with resultant radioactive decay helping in the diagnosis and treatment of a disease. NM considered as an autonomous imaging modality by World Health Organization (WHO) and is defined as combining altogether applications of different radioactive materials in the diagnosis or treatment of the disease, and in research in the field of medicine (1).

NM has become a cutting-edge specialization in all the medical areas and its various entities like Positron Emission Tomography (PET) and Single Photon Emission Computed Tomography (SPECT) hold immense potential for diagnosis and treatment information, including in the field of dentistry (2). NM involves injecting of radioisotopes, followed by the acquisition of images using specialized gamma camera, once the distribution and quantification of radioisotopes occurs, and works on the principle of metabolic activity (3). There is a lack of awareness among dental practitioners when it comes to basic uses of NM in the field of dentistry and it is underutilized in the region of head and neck pathologies. It is recommended that the diagnostic features of NM in the field of oral and maxillofacial region should be taken into consideration and the dentists should be provided with an insight regarding the various aspects of this specialized field of imaging for the perfection of diagnosis, treatment and proper follow-up.

Various Nuclear Imaging Techniques Scintigraphy

Scintigraphy produces two-dimensional images due to radiation emitted from an organ, injected with a radioisotope. The radioisotope emits characteristic radiation captured by specialized external gamma cameras. Scintigraphy has achieved a huge significance in the recent times, particularly in the imaging of bone and salivary glands (4).

Positron Emission Tomography (PET)

PET utilizes radioisotopes that emit the positron, for the biological or metabolic studies in the various organs of interest. 18F-fluorodeoxyglocose (18F-FDG) is the radiopharmaceutical most commonly used in PET scanning. PET has attained a great significance in the recent times for diagnostic and prognostic purposes in the region of head and neck malignancy. The advent of PET

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and its significant success as a diagnostic specialization, success of staging of nodes and tumors, assessing the benefits of therapy and monitoring of recurrence has raised an acclaim for increased consideration of advanced imaging in the field of health sciences (5).

Single Photon Emission Computed Tomography (SPECT)

SPECT uses single photon gamma-ray emission as the source of information, in contrast with the conventional computed tomography which relies on transmission of X-rays. SPECT and PET resemble in the use of radioactive tracers and gamma ray detection (6). SPECT differs from PET in that gamma radiation is emitted and measured directly, where as in PET positrons are emitted, and these annihilate with electrons, resulting in the release of two photons in the opposite direction and at an angle of 1800 to each other (4).

Fusion Imaging (PET-CT, PET-MRI, SPECT-CT)

NM images have limited resolution power, and such limitations pose difficulty in defining the accurate anatomical location of the disease (7). Fusion imaging overcomes these limitations by combining functional and molecular imaging provided by NM and anatomic imaging provided by computed tomography/magnetic resonance (CT/MRI). SPECT/CT fusion imaging advantages were seen in 38 patients with head and neck melanomas when it showed 16% additional sentinel nodes and showed a precise anatomical location of all the nodes (4). Fusion of PET and CT has proven its efficacy in diagnosing malignancies of head and neck at initial stages and thus enabling early treatment interventions for better prognosis. PET/CT has been particularly of significant importance when it comes to staging of head and neck squamous cell carcinoma, and monitoring the response to the treatment (8).

Radio Isotopes

Isotopes are elements that have a same atomic number but differ in their atomic masses, therefore contain a same number of protons but different number of neutrons. These elements being unstable undergo decay and emit energy as alpha(α), beta(β), beta plus(positron) and gamma-rays and are thus called as radioisotopes (9). These radioisotopes are also called as radionuclides. These isotopes are used in various sectors, and when used in healthcare system they are referred to as radiopharmaceuticals (10). There are about 1800 isotopes present but only up to 200 of them are in use currently, and most of them are manufactured by artificial means (9).

Radioisotopes are manufactured in many ways, the most common being in a nuclear reactor, while some of them are activated in a cyclotron. Technetium-99m, iodine-123, iodine-131, gallium-67 and thallium-201 are the most common radionuclides used in the liquid form whereas xenon-133, krypton-81m, technetium-99m and diethylene-triamine-pentaacetate (DTPA) are the most commonly used gaseous/aerosol forms. The following radionuclides are most commonly used for the maxillofacial pathologies. (11). Technetium-99m: Tumors of salivary glands, Gallium-67: Detection of osteomyelitis in the jaws. 18F Fluorodeoxyglucose(FDG): Malignant tumors in the maxillofacial region. The various radioisotopes used in the field of health care are shown in Table 1 (1) and Table 2 (1).

Table 1. Radioisotopes manufactured in a nuclear reactor

Reactor Radio-Isotopes	Uses
Technetium 99 m	To image the skeleton and heart muscle in particular, but is also used for brain and thyroid imaging
Cobalt 60	For external beam radiotherapy and used for sterilizing
Iodine 125	In cancer brachytherapy
Iodine 131	Used in imaging the thyroid function and thyroid cancer treatment
Iridium 192	Acts as source in internal radiotherapy for cancer treatment
Molybdenum 99	Used to produce technetium 99 m
Palladium 103	For brachytherapy in cases where early stage of cancers is detected
Strontium 89	For pain relief in osteochondromas
Caesium, gold and ruthenium	In brachytherapy as a treatment modality

Table 2. Radioisotopes manufactured in a cyclotron

Cyclotron Radioisotopes	Uses
Carbon 11, nitrogen 13, oxygen 15, fluorine 18	Used in PET scans through use of F 18 in FDG which help to detect, diagnose and know the prognosis of a tumor
Cobalt 57	Can be used as a detector for hypertrophy of cells, which indirectly determine the division and progression of cell growth to a stimulus
Copper 64	Is being used in PET scans and to check for the metabolism of copper
Copper 67	Used as an isotope for radiotherapy
Fluorine 18 as FLT (fluorothymidine), F miso (fluoromisonidazole), 18F choline	Used as traces, in radiotherapy
Gallium 67	For imaging of tumor size
Gallium 68	Used in PET scan to detect the metastatic activity
Germanium 68	Used to generate Ga
Rubidium 82	Used in PET scan to detect the cardiac myopathies
Strontium 82	Used to generate Rb 82

FDG: 18F Fluorodeoxyglucose, PET: Positron emission tomography,

Uses of Nuclear Medicine In Dentistry

The NM imaging can be utilized for a considerable number of applications in the field of dentistry owing to its ability to detect metabolic activities of hard tissues encompassed in the maxillofacial region. The minute radiopharmaceuticals injected can be correctly measured and distinguished from the inert masses in hard tissues. Many problems of mineral exchange and calcification problems can be studied with ease. NM can be utilized for studies involving detection of caries, the disease of the periodontium, investigating fluorosis, microleakage of various dental materials, resorption of roots, endocrine and nutrition effects (12).

NM can be used to study many metabolic and inflammatory disorders, tumors of head and neck, salivary gland dysfunction and many more other diseases afflicting the oral and maxillofacial region. Radionuclide imaging can accurately predict the ongoing disease process of an organ, well before any morphological changes have taken place (1). We put an effort to acquaint dental professionals about various possible indications of NM imaging in the region of head and neck.

Bone Scanning

The diseases of hard tissues of head and neck region are successfully evaluated using conventional and digital radiographs, and these imaging modalities continue to be the most readily available radiographic techniques. In certain diseases of the bones where pathology process starts way before any anatomical changes, the bone scan has a unique advantage of recording early biochemical changes, over other imaging modalities. The bone scan shows any early osteoblastic changes with precision, which otherwise does not appear on radiographic images. Barring the low resolution of bone scan images, it has an excellent osteoblastic detecting capability even in cases of as low as 10% increase in such activity (13). Two-dimensional images are captured following injection of radioisotopes, utilizing emitted characteristic radiation captured by external gamma cameras. The regions of high uptake of radiotracer are called as 'hot spots' whereas the areas with less or no uptake are called as 'cold spots.'

Technetium-99m labelled with diphosphonates (radiopharmaceutical) with a half-life of 6 hours is used in bone scans. The uptake of diphosphonates correlates with the degree of mineralization owing to its 40-fold affinity to hydroxyapatite than organic matrix (14). An even uptake of the radiopharmaceutical with symmetrical fashion around the midline depicts a normal bone scan. The various bone scan techniques include Standard Bone Scan, 3-Phase Bone Scan, and SPECT.Standard bone scan employs capturing of static images 3 hours after injection of a radiopharmaceutical. Such deferred acquisition of static images may be diagnostic in cases of condylar hyperplasia. The 3-Phase study comprises a flow assessment, a blood pool image, and delayed static views acquisition. This technique is performed to gain extra information in cases where, distinguishing osteomyelitis and cellulitis is important for diagnosis and usually employed for evaluating, inflammatory disorders, trauma, and primary bone tumors.

- Rapid successive images are acquired for 60 seconds through intravenous administration of the radiotracer during the dynamic flow study, which allows assessing differences in vascularity on each side.
- This is followed immediately by the acquisition of image through a stage of tissue hyperemia, called as the blood pool image. In this stage, the radiopharmaceutical is concentrated mostly in vascular compartment and just begins to appear in the skeleton. This phase reveals local differences in blood flow and vascular permeability.
- The bony uptake of technetium-99m labelled diphosphonate peaks at 3 hours after the injection of the radiopharmaceutical, with most of the unbound radiotracer excreted through kidneys at this period. This stage of maximal uptake of the radiopharmaceutical is suitable for the last delayed static image.

There is increased uptake of radiopharmaceutical in metabolic diseases like fibrous dysplasia and Paget's disease (15). Bone scan can give conflicting results in cases of active periodontal disease with an increased uptake of radiopharmaceutical in the alveolar processes. Such confounding observations can also be seen in cervical spine showing increased uptake in cases of arthritis and growing kids when they show uptake in epiphyseal regions (16). Certain inflammatory conditions of temporomandibular joints(TMJ) can show increased uptake similar to that of condylar hyperplasia and requires careful assessment of history, clinical examination, laboratory and radiographic information for a precise diagnosis.

The bone scan also shows lesions with decreased uptake, so called Photopenic areas, common among them being early osteomyelitis, local vascular compromise, radiation treatment, prosthetic joint, avascular necrosis and multiple myeloma. A Bone scan can also show soft tissue activity in the region of head and neck and following conditions should be taken into consideration, chronic inflammatory changes, hyperthyroidism, hematomas, dystrophic calcifications, infarction and renal failure (17).

Bone scanning can also be done utilizing SPECT. SPECT involves, acquisition of 64 projections of rotating delayed static images, which are then reconstructed in a computer to provide three-dimensional multiplanar slices in axial, coronal and sagittal planes of the area of interest. SPECT can find use in the region of TMJ disc derangements (12). The evaluation of TMJ disorders using SPECT gives comparable results with that of MRI (18,19).

Scintigraphy of Salivary Glands

Salivary gland scintigraphy involves the use of scintillation crystals for acquiring data for image acquisition. The widely known radiopharmaceutical technetium 99m pertechnetate mimics, the influx of chloride into the acinar cells of functioning parenchyma of major salivary glands and thus establishing the basis of this imaging modality (20). The procedure entails injecting of radiopharmaceutical and recording the resultant distribution utilizing scintillation camera. This is a means of evaluating mass lesions and functional evaluation of salivary glands (16). The further uses of this scintillation technique in salivary glands include assessing obstructive disorders, distinguishing agenesis and aplasia, traumatic lesions, and salivary gland functioning post-operatively.

Except for Warthin's tumor and oncocytomas which show increased uptake and decreased washout time of the radiopharmaceutical all other mass lesions of salivary glands show decreased uptake of the radiotracer. Acutely inflamed salivary glands demonstrate increased uptake and increased washout time, whereas it is decreased uptake in cases of chronic glandular inflammation (21). Radiopharmaceutical is poorly up taken in Sjogren's syndrome (16).

Gallium Scan

Gallium-67 (67Ga) is one among the number of radioisotopes used in the imaging of tumors, infection, and inflammation (22). After intravenous administration of 67Ga citrate, its nonspecific accumulation in the areas of infection, inflammation and neoplastic tissues allows image acquisition and can be used for diagnostic purposes due to its affinity for rapidly dividing cells like white blood cells and other tumor cells (23). 67Ga scans having mostly been replaced by 18F-fluorodeoxyglucose PET/CT scintigraphy in the assessment and follow-up of lymphoma patients, are still in use in places lacking PET/CT facilities (24). 67Ga is useful in the evaluation of suspected osteomyelitis. As 67Ga has a half-life of 78 hrs, technetium (half-life 6 hrs) scan should be performed first if both are planned (25). A positive 67Ga scan with associated technetium uptake is highly indicative of osteomyelitis. A normal 67Ga scan with a positive or normal bone scan is not suggestive of an infection. A resolving osteomyelitis shows a decreased uptake of 67Ga and thus helps in monitoring the response to treatment.

Nuclear Imaging In Head And Neck Cancer

Head and neck cancer (HNC) occurs in 6,50,000 individuals every year throughout the world (26). Head and neck squamous cell carcinoma (HNSCC) has high recurrence rates and constitutes about 90% of all HNC. There is always a need for better imaging modalities for diagnosis, staging, treatment designing, evaluating response and envisaging result when we are dealing with diseases of such burden. Among such advanced imaging modalities, FDG PET/CT radiotracer imaging is one of the valued modality (27). FDG-PET/CT gives convincing results in detecting tumor size and shape, occult primary tumors, locoregional nodal spread, and distant metastases (28-30). In its updated version of guidelines of 2013 National Comprehensive Center Network (NCCN), clinical practice guidelines in HNC favor PET/ CT scans in the initial staging of patients with stages III and IV disease of the oral cavity, oropharynx, hypopharynx, and larynx (31). Precise staging of tumors leads to reliable decision making and also avoids pointless interventions during the course of the disease (29). FDG PET/CT delivers a correct staging in HNCs than conventional work-up and may modify the treatment plan (32). As 18F-FDG-PET tracks metabolic action of neoplastic cells, FDG PET plays a significant role in assessing the response to the treatment (28,33).

Lymphoscintigraphy

Lymphoscintigraphy involves the acquisition of plane and tomographic images after injecting of a suitable radiopharmaceutical usually technetium 99m through lymphatics. The goal of lymphoscintigraphy is to identify and localize all sentinel lymph nodes(SLNs) for surgical biopsy (34). The SLN is the first lymph node receiving drainage from the primary tumor. In case the SNL has no signs of any malignancy, the remaining lymph nodes are highly likely to be negative as well (35). The removal of only the SLNs eradicates the need for the removal of other lymph nodes and thus reduces the accompanying side effects and thus improves prognosis. Sentinel lymph node biopsy (SLNB) holds promise in HNSCC. SLNB is used for staging of lymph nodes and is the gold standard in melanoma and breast cancer. SLNB has been seen to disclose 15% to 60% occult metastasis in squamous cell carcinoma (SCC) of the oral cavity, pharynx and that of supraglottis. Numerous studies have confirmed the decent results of SLNB in HNSCC (36).

Nuclear Imaging In Tissue Engineering

The functional characterization of stem cells within a critical-sized bone defect has been studied using 18F-FDG-PET, and such imaging when combined with CT gives additional information about the mechanical integrity of bone (37). PET imaging has been used to evaluate the osteogenic metabolism of the genetically engineered bone marrow-derived mesenchymal stem cells for repairing of critical-size bone defects (38). The fusion imaging consisting of PET/CT or SPECT/CT coupled effectively with many shared components provides the advantage of functional imaging (PET, SPECT) plus additional structural information furnished by CT. In molecular imaging, in vivo PET shows an increase of matrix metalloproteinase and CT gives an idea about bone formation changes at various stages after bone morphogenetic protein (BMP)-induced cell injection (39).

Advantages And Disadvantages of Nuclear Medicine (40)
Advantages

- NM imaging has an advantage of providing anatomical details and information that helps in accurate diagnosis
- NM imaging is based on the principle of tracers and shows functional images of metabolism, physiology or biochemistry by studying the dynamic behavior of tissues and organs at various stages.

- It can help in early diagnosis of the disease and evaluates the outcome during the initial post-treatment phase.
- By allowing easy demonstration of whole body images and active display, NM helps in detecting metastatic activity.
- Different regions of the body can be examined at varied times using a single injection of radioisotope in NM imaging without any increased radiation dose, which is unlike other conventional techniques that need a number of exposures for examining different anatomical locations

Disadvantages

- The spatial resolution in NM imaging is reduced when compared to other imaging modalities like MRI or CT.
- Ionizing radiations are used in NM, and the patients have a risk of being exposed to higher doses of radiation.
- It's comparatively expensive, and the cost varies according to the choice of radiopharmaceutical used.
- The staff handling patients for NM imaging are at a higher risk of radiation exposure and thus a minimum of 6mm of lead shielding is recommended.

CONCLUSION

Nuclear Medicine(NM) imaging is a non-invasive imaging modality which has a potential of detecting various pathologies in the region of head and neck with a high sensitivity and specificity rates. The different imaging modalities that are routinely used in the health care system are morphologic imaging techniques, in that a macroscopic change in the anatomy is required for any diagnostic information. NM has an advantage over all such imaging modalities as it records abnormal biochemical processes even in the absence of any anatomical changes in the body. The ability to measure such biochemical changes allows NM imaging to provide an early marker of the disease. It is important for dental professionals to take advantage of this prophetic imaging modality and keep themselves abreast with its various principles as they may be required at times to interpret and discuss pros and cons associated with this functional imaging modality.

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