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Derleme

Nuclear Imaging Applications in Dentistry

Diş Hekimliğinde Nükleer Görüntüleme Uygulamaları

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ABSTRACT

This review aims to discuss the indications, limitations, and diagnostic implications of nuclear imaging in the oral and maxillofacial region. In contrast to conventional imaging modalities in dentistry, such as panoramic radiography and cone beam computed tomography, nuclear medicine offers unique information specific to the functional aspects of oral and maxillofacial tissues. In addition, by emphasizing the current and potential applications of nuclear imaging methods in dentistry, it is also aimed to increase the level of knowledge of dentists on functional imaging methods and gain a different perspective, along with their effects on diagnostic accuracy, treatment planning, and treatment outcomes. Future research will allow a detailed evaluation of the effectiveness and reliability of nuclear imaging technologies in dentistry.

Keywords: Dentistry, Molecular Imaging, Positron-Emission Tomography, Single-Photon Emission Computerized Tomography

ÖZET

Bu derlemenin amacı oral ve maksillofasiyal bölgede nükleer görüntüleme endikasyonlarını, uygulama ile ilgili sınırlamaları ve tanısal sonuçlarını tartışmaktır. Diş hekimliğinde geleneksel görüntüleme yöntemleri olan röntgen ve konik ışınlı bilgisayarlı tomografi yöntemlerine karşılık, nükleer tıp, ağız ve çene-yüz dokularının fonksiyonel yönlerine özgü eşsiz bilgiler sunmaktadır. Ayrıca nükleer görüntüleme yöntemlerinin diş hekimliğinde mevcut ve potansiyel uygulamaları vurgulanarak, teşhis doğruluğu, tedavi planlaması ve tedavi sonuçları üzerindeki etkileri ile birlikte diş hekimlerinin de fonksiyonel görüntüleme yöntemleri üzerindeki bilgi düzeylerini arttırmak ve farklı bir bakış açısı kazandırmak da amaçlanmıştır. Gelecekte yapılacak araştırmalar, diş hekimliğinde nükleer görüntüleme teknolojilerinin etkinliği ve güvenirliliğinin detaylı bir şekilde değerlendirilmesine olanak sağlayacaktır.

Anahtar Kelimeler: Diş Hekimliği, Moleküler Görüntüleme, Pozitron Emisyon Tomografisi, Tek Foton Emisyon Bilgisayarlı Tomografi

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INTRODUCTION

Nuclear medicine is a specialty in which radioactive materials are used to evaluate body functions and diagnose and treat diseases. Medical imaging methods can be classified into two different types: transmission and emission imaging. Transmission imaging uses an external X-ray source, such as digital or conventional radiography and Computed Tomography (CT) imaging techniques. Emission imaging methods, also called nuclear imaging, show the function of organs and tissues by emitting photons at sites of biochemical activity using internal radionuclides. Nuclear imaging has a wide range of clinical applications in cardiology, oncology, neurology, and many other fields, such as diagnosing various conditions and diseases, evaluating response to treatment, and monitoring diseases. This method has various clinical applications, such as determining disease spread, evaluating treatment response, and monitoring disease progression with repeated scans.[1] Nuclear medicine applications also play an essential role in diagnosing and treating oral and maxillofacial diseases. This review aims to provide a broad overview of nuclear imaging modalities and evaluate their application in diagnosing and treating oral, dental, and maxillofacial diseases.

While transmission imaging aims to visualize anatomical structures using X-rays, nuclear imaging aims to obtain functional images of organs and tissues using low-radioactivity agents. However, nuclear imaging has its drawbacks. In particular, the radiation emitted by radionuclides can cause concerns among nuclear medicine professionals, healthcare workers, and the general public. In addition, the limited dose of radioactive materials used for nuclear imaging limits the resolution of the images obtained. Furthermore, nuclear imaging modalities are costly procedures and require specialized equipment and trained personel to perform them.[2]

Radionuclides and Radiopharmaceuticals

In nuclear medicine, radionuclide elements in scans and treatment are combined with a carrier molecule and converted into a form suitable for injection into living tissue. Radioactive compounds in this form are called radiopharmaceuticals. Radiopharmaceuticals are injected into the patient's body; sensitive detector systems detect the radiation produced by the decay of these substances; images are obtained. In nuclear medicine, clinical information is received by visualizing the distribution of a pharmaceutical substance in the body.[3] The most commonly used radiopharmaceuticals and radionuclides are given in Table 1.[1]

Radiopharmaceuticals are radioactive compounds directed to the targeted tissue for therapeutic or imaging purposes thanks to their radionuclides. These compounds are created using radionuclides that have the desired imaging properties. Various radionuclides are usually used in the production of different radiopharmaceuticals. The choice of radiopharmaceutical varies depending on the organ to be imaged and the pathology under investigation. Radiopharmaceuticals used in nuclear imaging are divided into single-photon emitters and positron emitters. Single Photon Emitters emit gamma rays to

Table 1. Table showing the most commonly used radiopharmaceuticals and radionuclides in nuclear medicine applications and their areas of use.[1]

Radionuclide	Radiopharmaceutical	Area of Use
Flor-18	FDG (Fluorodeoxyglucose)	Tumor, Infection, Cardiac Viability, and Brain Metabolism
	Sodium	Bone
Gallium-67	Citrate	Infection, Tumor
Technetium-99m	Diphosphonate	Bone
	HMPOA- labeled white cells (hexamethylpropyleneamine oxine)	Infection
	Pertechnetate	Thyroid, Salivary glands, and Meckel's cartilage
Indium-111	Oxine labeled white cells	Infection
Iodine-123	Sodium	Thyroid
Iodine-131	Sodium	Thyroid cancer

visualize the tissue. This method is performed using detectors such as gamma cameras. Positron-emitting radionuclides are used in Positron Emission Tomography (PET) imaging. Both groups of radiopharmaceuticals have different applications in nuclear imaging.[3,4]

Scintigraphy

Gamma cameras are devices used for medical imaging that detect gamma rays emitted by radioactive isotopes. They are used in nuclear medicine to produce images of the distribution of radioactive isotopes in the body. Using scintillation crystals to acquire data for image formation has led to the technique called Scintigraphy.[1,5]

Scintigraphy is less successful than radiograms in showing the fine structure of bone. Still, it is used in the diagnosis and localization of malignant tumors, metabolic diseases, trauma, pulmonary anomalies, and cardiac diseases.[6,7] Most pathological processes affecting bones are associated with increased bone metabolism or new bone formation. Radionuclide bone scanning detects what appear to be "hot spots," areas of increased uptake of radioactive substances in areas of increased bone metabolism. These areas indicate the presence of pathological processes or increased bone activity. On the other hand, so-called "cold spots," areas of reduced or absent uptake, appear in metabolically inactive regions or areas of incomplete bone formation. The inorganic structure of bone is mainly composed of calcium, phosphate, and hydroxyl ions, which form hydroxyapatite. The radiopharmaceuticals used in bone scanning are analogs of calcium, hydroxyl groups, or phosphates. The most commonly used radiopharmaceutical for skeletal scintigraphy is Technetium-^{99m}-Methylene Diphosphonate (Tc-MDP ^{99m}).[1] Conventional radiography requires 40% to 50% decalcification to detect a change in bone, whereas Nuclear Imaging can detect a 10% change. Nuclear imaging can detect lesions earlier and faster than conventional radiography.[8] Radionuclide bone scanning is an effective imaging method for diagnosing and evaluating bone diseases. This scan identifies pathological bone processes, guides the treatment process, and helps detect the disease's spread.

Areas of Use in Dentistry

Scintigraphy is used to detect the spread of cancer cells into bones and has a high sensitivity in detecting metastatic lesions. Bone scintigraphy has also been used successfully to evaluate vascularized bone grafts for maxillofacial reconstructions.[9] Bone scintigraphy is useful in assessing inflammatory lesions, infections, and conditions such as fibro-osseous dysplasia. Scintigraphy is used to detect such lesions' localization, extent, and activity. It offers high sensitivity, especially in detecting chronic infections and inflammatory processes. Bone scintigraphy is considered an effective tool in evaluating various pathological conditions and is a widely used imaging modality in clinical practice.[8]

Temporomandibular Joint (TMJ) diseases such as osteoarthritis lead to changes in bone metabolism. The affected areas can, therefore, be visualized in bone scans. Scintigraphy is useful in detecting changes in the skeletal system of the TMJ, joint disc abnormalities, and inflammatory diseases in their early stages.[10]

Nuclear medicine images can help diagnose and evaluate some salivary gland disorders. Salivary gland scintigraphy uses ^{99m}Tc Pertechnetate, which can replace Sodium or Potassium Chloride (Na-K-Cl) Chloride in the salivary transport pump, therefore, helps to measure fluid movement in the salivary acinar glands.[11-13] Santos *et al*. described monitoring salivary glands by scintigraphy before and after one percent pilocarpine administration in a patient with Sjögren's syndrome. The results showed that scintigraphy with ^{99m}Tc Pertechnetate assessed the affected localization, the progression of disease activity, and the severity of the glands involved.[14]

The ^{99m}Tc O4, Gallium (67 Ga) Citrate scintigraphy together show the function of the salivary gland and are used in the diagnosis of common diseases, such as Sialadenitis, Sjögren's syndrome, and Sarcoidosis.[14,15]

Bone scans are used to assess bone viability in cases with different clinical manifestations, such as septic embolism, avascular necrosis, frostbite lesions, and osteonecrosis, and evaluate surgical treatment outcomes in patients with avascular necrosis. The 18F-fluoride PET and the ^{99m}Tc-MDP bone scans demonstrate bone viability by showing vascular nutrition and osteoblast activity and are accurate tools for early assessment of bone graft viability.[16-18]

Single Photon Emission Tomography (SPECT)

Single Photon Emission Tomography (SPECT) was developed to eliminate the planar image formation, one of the most important disadvantages of scintigraphy imaging, and obtain three-dimensional images similar to tomography. In SPECT systems, single or multiple gamma cameras move around the patient in a 360^{O} rotation similar to tomography, and gamma rays are emitted to form an image.[19]

The main advantage of SPECT systems is using the same radiopharmaceutical agents as scintigraphy to obtain superposition-free images. Therefore, pharmaceutical agents are more accessible and less costly than PET systems.

Areas of Use in Dentistry

TMJ diseases: The use of ^{99m}Tc-MDP SPECT/CT allows MDP uptake in the bones that make up the TMJ to be correlated with the morphologic changes visualized on CT. SPECT imaging is more successful than TMJ scintigraphy in symptomatic TMJ diseases, detecting inflammatory arthritis at an early stage and identifying the disease without morphologic and radiographic changes.[20] In another study, ^{99m}Tc-MDP SPECT/CT image fusion was found to diagnose TMJ irregularities in 90% of patients accurately, and the sensitivity, specificity, and accuracy of this method were 90%, 95%, and 92.5%, respectively.[21] SPECT/CT is useful in prognostic assessment or determining treatment strategies for idiopathic condyle resorption and degenerative joint disease.[22]

Condylar Hyperplasia: Condylar Hyperplasia (CH) is a condition that occurs as a result of excessive growth of the mandibular condyle. This growth can cause facial asymmetry, jaw deviation, jaw pain, mouth opening restriction, and chewing difficulty.[23]

In patients with CH, treatment depends on the status of the growth. However, CT and Cone Beam CT (CBCT) often cannot determine this status; thus, functional imaging techniques must be used. SPECT can detect the presence of active growth and remodeling. These techniques are essential in deciding growth activity; in particular, a bone scan with more than 10% involvement of one condyle compared to the contralateral condyle supports the diagnosis of unilateral growing CH. However, it cannot be distinguished from inflammatory, infectious, tumoral, or healing processes. Therefore, the results should be evaluated with clinical findings and anatomical imaging. Quantitative evaluation by assessing the Standardized Uptake Values (SUV) in regions involving both condyles helps define the treatment course. SPECT/CT13 and F-fluoride PET/CT can help diagnose CH and determine appropriate management.[24-27]

SPECT/CT joint imaging is a promising alternative for evaluating internal joint irregularities in patients with contraindications to Magnetic Resonance Imaging (MRI) and metallic implants.[28]

Osteomyelitis: MRI and CT are sensitive for assessing the location, extent, abscess formation, osteomyelitis, airway narrowing, and possible complications of soft tissue infections. Three-phase bone scintigraphy can determine osteomyelitis earlier than CT, while SPECT/CT detects osteomyelitis at an early stage and gives better results in the follow-up of treatment compared to CT and Panoramic radiography.[29]

Positron Emission Tomography (PET)

Positron Emission Tomography (PET) imaging is an advanced imaging method in nuclear medicine. The most important difference from other radionuclide imaging methods is using positron-emitting radionuclides instead of gamma-ray-emitting radionuclides. The superiority of PET imaging is related to the physical properties of the positron. After losing most of its kinetic energy, a positron reacts with an electron in the environment. This reaction produces two gamma photons with 511-keV energy emitted in opposite directions.[1] PET imaging works with these simultaneously generated gamma photons. Electronically coupled detectors detect the simultaneous photon pairs, and the emitted gamma photons are recorded simultaneously. The position of the radionuclide is thus determined by the intersection of the detector pairs recording the simultaneous events. While gamma cameras only detect gamma photons emitted in one direction, PET systems can simultaneously detect photons emitted at the same point and traveling in opposite directions, which allows

PET systems to provide absolute three-dimensional localization of the radiopharmaceutical distribution, quantification, and three-dimensional visual representation of the imaged organ. PET can detect minor and less aggressive tumors that other radionuclide imaging modalities cannot and is suitable for staging and follow-up of cancers.[30]

Areas of Use in Dentistry

Malignant diseases, TMJ disorders, condylar hyperplasia, infection, osteomyelitis, Biphosphonate-related osteonecrosis of the jaw (BRONJ), Sjögren's syndrome, Paget's disease, SAPHO syndrome, and bone graft viability are the main uses in dentistry.

Malignant Diseases: PET/CT provides higher sensitivity and specificity in staging squamous cell carcinomas compared to contrast-enhanced CT or MRI. After treatment, FDG-PET/CT can assess the response earlier and more accurately to identify biochemical changes in tumor metabolism before morphological changes. When anatomy changes, it differentiates between benign and malignant diseases, particularly after surgery.[31] PET data provide important prognostic information for more personalized surveillance and treatment planning. High FDG uptake is associated with poor prognosis and poorly differentiated tumors. PET-based radiotherapy planning offers more accurate and generally smaller radiation fields than those based on contrast-enhanced CT.[16, 32, 33]

PET provides high sensitivity in identifying recurrent, metachronous, and synchronous tumors. FDG-PET/CT can localize the primary tumor in 22% to 44% of patients with head and neck cancer of unknown primary. Similarly, FDG-PET/CT is more sensitive and specific than contrast-enhanced CT in the evaluation of lymphoma, melanoma, and metastatic disease to the maxillofacial region.[16]

A meta-analysis of seven studies of 687 patients comparing bone marrow biopsy with FDG-PET to detect bone involvement due to Hodgkin's disease showed that both methods had high specificity.[34] Still, the sensitivity of PET was 94.5%, and that of bone marrow biopsy was 39.4%, meaning that PET had a higher diagnostic power to detect bone marrow involvement.[16,34]

FDG-PET/CT imaging is highly successful in detecting cervical lymph node metastasis in patients with newly diagnosed and untreated oral squamous cell carcinoma. It is a valuable tool to optimize the treatment of these patients and detect distant metastases.[35]

FDG-PET/CT is recognized as an essential imaging modality for staging, evaluation of treatment response, and restaging of primary lymphoma and certain metastatic neoplasms of the head and neck. It has also been used effectively for initial staging, treatment evaluation, and post-surgical follow-up of multiple myeloma, malignant ameloblastoma, and ameloblastic carcinoma.[16]

Temporomandibular Joint Disorders and Diseases: Studies to differentiate osteoarthritis of the TMJ and anterior disc displacement have shown that 18 F-PET scanning has higher sensitivity and accuracy than ^{99m}Tc-MDP bone scanning. In addition, 18 F-NaF PET/CT is a valuable imaging tool for evaluating and treating TMJ irregularities. Studies have found that Maximum Standard Unit Value (SUVmax) for TMJ irregularities correlates with reasonable diagnostic performance and therapeutic response for conditions such as arthralgic TMJ and TMJ osteoarthritis.[36,37]

Infection, Osteomyelitis: Marked Leukocyte SPECT/CT or FDG-PET/CT scanning is preferred in suspected osteomyelitis areas. In a study,18 F-FDG-PET and 18 F-Fluoride-PET imaging provided different information about jawbone metabolism and inflammation. Therefore, the combined use of both methods was determined to be more accurate in terms of showing the true activity of osteomyelitis. 18F-FDG-PET shows infection, and 18 F-Fluoride-PET shows areas of bone remodeling.[38]

Bisphosphonate Related Osteonecrosis of The Jaws (BRONJ): Studies have shown that MDP uptake correlates with the BRONJ stage, and it has been emphasized that this may have a prognostic value. Due to better spatial resolution, correlation with CT findings, and multi-planar image evaluation, 18F-Fluoride PET/CT is more specific and sensitive in detecting BRONJ than^{99m} Tc-MDP bone scan. Furthermore, 18F-Fluoride PET is more accurate than contrast-enhanced MRI, CIBT, and Panoramic images. To show the severity of BRONJ and response to treatment, 18F-FDG-PET is utilized.[39-41]

Sjögren's Syndrome: Primary Sjögren's syndrome (pSS) is an autoimmune disease characterized by dry mouth and eyes. Imaging techniques such as sialography, MRI, sialendoscopy, salivary gland scintigraphy, and PET are used to diagnose and monitor pSS. These modalities help to diagnose pSS, assess disease activity, and analyze and stage associated lymphomas. Nuclear imaging modalities can be instrumental in the diagnosis and staging of pSS. Despite the limitations of conventional nuclear medicine, PET, when combined with CT, provides better spatial resolution and the ability to quantify tracer uptake. FDG-PET/CT can be an alternative to invasive biopsies in patients with suspected pSS-associated lymphoma and can detect systemic manifestations and guide biopsy location.[42-44]

Paget's Disease: Paget's Disease is usually diagnosed by typical radiographic findings such as coarsening of the trabecular pattern and subperiosteal cortical thickening. However, radiography may underestimate the extent of the disease as scintigraphy shows the transformation of normal bone into diseased bone before the radiographic changes become apparent. In a study comparing radiography, bone scintigraphy, and F-18 FDG PET/CT imaging findings in Paget's disease, PET/CT has been shown to have a higher sensitivity in detecting bone involvement and can detect earlier stages of the disease more successfully than bone scintigraphy.[45]

Since PET/CT is non-invasive and provides quantitative measurements, it can also be used in treatment planning and follow-up of response to treatment in Paget's disease.[46]

SAPHO Syndrome: Synovial Aseptic Pyodermatosis and Osteomyelitis (SAPHO) and Chronic Reactive Arthritis and Osteomyelitis (CRMO) diseases are characterized by synovial and bone involvement. Radiography is the most commonly used imaging modality, showing findings including bone sclerosis, erosion, and sclerotic bone plaques. On the other hand, bone scintigraphy effectively identifies bone involvement in the joints, especially in early diagnosis. In addition, PET/CT detects increased glucose metabolism at early diagnosis and provides a detailed assessment of the disease, which may include bone sclerosis, erosions, and sclerotic bone plaques. Bone scintigraphy shows areas of hyperostosis and osteitis, which in some cases are not visible on radiographs. In addition to revealing more occult lesions and active inflammation, 18F-FDG PET/CT scanning can effectively exclude neoplastic lesions, detect areas of synovitis, and more successfully demonstrate SAPHO syndrome than planar scintigraphy.[47,48]

CONCLUSION

Nuclear imaging applications play an essential role in dentistry by contributing to the diagnosis and treatment processes. These technologies can enrich the practice of dentistry by offering the potential to obtain more precise and detailed information. Future research will increase knowledge in the field by examining the effectiveness and reliability of nuclear imaging technologies in dentistry in more detail.

The studies conducted in this framework are expected to contribute significantly to the literature and create a clearer understanding of the future use of nuclear imaging applications in dentistry.

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CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

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