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Chapter

Emerging Role of Nuclear Medicine in Oral and Maxillofacial Surgery

Tina Nazerani, Peter Kalmar and Reingard M. Aigner

Abstract

During the past several years, nuclear medicine has emerged as one of the most useful imaging studies in oral and maxillofacial surgery, not only in diagnosis and staging but also in the management plan and follow-up protocols of many cancer or inflammatory diseases. Nuclear medicine has in addition a special place in treating several benign and malignant diseases. The practicing maxillofacial surgeon's knowledge of nuclear medicine capabilities and advantages and disadvantages of each modality is crucial in his or her daily work. The purpose of this chapter is to clarify the important role of nuclear medicine in diagnosis and treatment of oral and maxillofacial region pathologies as well as its indications and limitations in the daily practice of the oral and maxillofacial surgeon.

Keywords: nuclear medicine, maxillofacial surgery, oral cancer, bone scintigraphy, SPECT/CT, sentinel lymph node, F18-FDG, PET/CT

1. Introduction

Nuclear medicine has become one of the essential diagnostic tools in all fields of medicine, and one of these fields is oral and maxillofacial surgery. As an independent specialty, it is characterized by the injection of radioactive labeled materials to identify the presence and location of primary and metastatic cancer, inflammatory diseases, etc. Advanced imaging procedures such as positron emission tomography (PET) combined with computed tomography (CT) as well as single-photon emission computerized tomography (SPECT) and sentinel lymph node scintigraphy have shown to be precise diagnostic tools in oral/maxillofacial pathologies; however its importance and role in diagnosis of pathological conditions need to be discussed more and better presented to other medical and surgical disciplines [1].

In comparison to other morphological imaging modalities such as CT, magnetic resonance imaging (MRI), and ultrasonography, biochemical changes in different tissues of various pathophysiological processes are diagnosed earlier by radionuclide imaging through the injection of radioactively labeled substances [2].

2. A short journey throughout history

Chemistry Nobel Prize winner Georg Charles de Hevesy was the first to use radioactive isotopes to study the metabolic processes of plants and animals.

He observed the chemical activity of the animal body by replacing parts of stable isotopes with small amounts of radioactive isotopes. In 1923, he published his first study of radioactive tracer Lead-212 to observe the uptake of labeled ions by the different parts of horse bean. He carried out his experiments in animals with Bismuth-210, injecting it intramuscularly in rabbits to follow the dynamic behavior of the tracer. De Hevesy is often referred to as the father of nuclear medicine [3].

However, one must not forget that the history of nuclear medicine is full of contributions by other scientists such as Wilhelm Konrad Roentgen, Marie Curie, and Henri Becquerel.

Hermann Blumgart was the first to perform human use of radioactive tracers in 1925. He measured the "velocity of the circulation" by measuring the time it took the injected solutions of radon flow from one arm to another. George Moore, MD, a neurosurgeon at the University of Minnesota, performed the first brain study using Di-iodofluorescein to detect brain tumors [4].

Nuclear medicine's golden era of recognition by the medical community began in 1946, when it was described as a successful treatment of thyroid cancer using radioiodine (I-131). This is considered to be one of the turning points in the history of nuclear medicine [5].

The modern principle of nuclear medicine is based on the works of Benedict Cassena and Hal O. Anger for developing the first rectilinear scanner and scintillation camera. Three-dimensional reconstruction of the heart in the 1980s using SPECT has led to the establishment of nuclear medicine in cardiology by using radiotracers for the diagnosis of various heart diseases.

The most recent development is the invention of PET/CT. This modality plays a pivotal role in all stages of oncological diseases from pre-treatment staging to the follow-up protocols [6].

3. Statistics, etiology, and pathology of head and neck cancers

The core principle of every living creature is in the so-called condition of homeostasis, which allows biomolecules to balance themselves in a dynamic process. When homeostasis is disrupted, it can lead to an unbalanced situation or, in other words, disease. The tracers with similar chemical structures as the ones present in the body are used to understand and analyze the in vivo molecular situation of one organ or several organs.

The growing need for a precise diagnostic workup has led to a search for more center-based instead of disease-based patients.

Modern medicine today prescribes a complete survey of the disease process, locating cancer and possible metastatic growths, before taking an action, i.e., surgery or chemo-radioactive ablations.

According to the 2018 global cancer statistics, lip and oral cavity cancers are the leading areas of tumor involvement in the head and neck region. They are followed by nasopharynx, oropharynx, hypopharynx, and salivary glands. These types of cancer are more prevalent in men. Global incidence rate is higher in Southern Asia, especially in Sri Lanka and India, where it is the leading cause of death in male patients [7]. The risk factors for head and neck cancers are tobacco and alcohol [8–11]. The risk is even higher in cases using both alcohol and tobacco than cases using either alcohol or tobacco alone [12–14].

Squamous cell carcinoma (SCC) is the most common type of cancer in the head and neck region, with a rate of over 90%, and mostly found in the larynx and oral cavity. The other cancer types are salivary glands adenocarcinomas, melanoma, lymphomas, and rare tumors (e.g., paragangliomas) [15].

Nearly one third of patients are seen in early stages, while the remaining two thirds present in advanced stages.

Surgery and/or radiotherapy seems to be more useful in early stages; however, due to the high risk of recurrence and metastasis as well as the development of second primary cancer, the prognosis of these cases is also not significantly better [16].

Carcinogenic subtypes of human papillomavirus (HPV), especially subtype 16, are associated with some head and neck cancers commonly involving oropharynx, tonsil, and the base of the tongue [17–19].

Poor oral hygiene, preserved and/or salted foods, and occupational exposure to certain industrial materials such as asbestos are other risk factors in nasopharyngeal and laryngeal cancers. In addition, radiation exposure is a risk factor in salivary gland cancers. Epstein-Barr virus is responsible for cancer of the nasopharynx and salivary glands [20–23].

4. Imaging studies in nuclear medicine

The desire to find the best therapeutic management and oncologic regimens is undeniable. To exactly determine the stage of the cancer in head and neck area is indispensable to the oncological team for choosing the best treatment strategy as well as follow-up protocols.

Radionuclide imaging studies are as follows:

a. Bone scintigraphy

b. Statistics and indications

c. PET/CT scans

d. Lymphoscintigraphy

5. Bone scintigraphy in head and neck surgery

The bone is in a constant state of turnover as a result of metabolic or mechanical demands, and a fine balance is present between osteogenesis and bone resorption. Oral pathologies cause metabolic changes in the bone and surrounding structures of maxillofacial region; these changes can be due to trauma, infection, neoplasm, or other etiologies. These disease processes are associated with hypervascularization and biochemical changes of the bone and surrounding structures; therefore, it is of great value to use bone scintigraphy with its minimal radiation exposure to identify these disease processes.

The conventional X-ray is still the most convenient method for detection of pathologies affecting boney structure of the maxillofacial region. However, the changes are first seen when more than 30% of bone structure is involved.

On the other hand, morphological changes due to the biochemical processes of osteoblastic activities can be detected at the early stages of bone remodeling by bone scintigraphy [1].

Bone scintigraphy is a functional imaging study, whereas other anatomical modalities, such as CT or MRI, are structural studies.

Bone scintigraphy can detect osteoblastic activity with only a 10% change above the normal value. Although the quality and resolution of bone scans are not as

sharp as X-ray, abnormalities can be seen long before morphological changes. Bone scintigraphy is also helpful in cases with suspected non-vitality bone lesions.

Most of the pathological processes involving the bone are the result of new bone formation or increased turnover. These appear in bone scans as areas of increased tracer uptake, known as "hot spots."

Inactive metabolic conditions decreased or lack of new bone formation or reduced blood supply result in decreased tracer uptake showing either a disruptive reparative process or suggesting an aggressive lesion of nonconformity to the native tissues. "Cold spots" are areas with a lack of or reduced tracer uptake.

Bone scintigraphy is done by intravenous injection of Technetium-99m-labeled diphosphonate with 140 KeV gamma energy. It has a short physical half-life of 6 h with minimal radiation exposure.

A significant amount of unbound tracer is excreted in the urine. The tracer has a high ratio of up to 40% affinity to the hydroxyapatite.

Depending on the clinical diagnosis, there are different techniques for performing a bone scan. The "planar whole-body" images are the anterior and posterior acquisition of the skeleton. This includes static images 3–4 h after tracer injection. If necessary, an additional "spot view" can be obtained.

"Three-phase" bone scintigraphy consists of the blood flow and the soft tissue images and "delayed static images." Dynamic images are acquired during the intravenous injection of the tracer and demonstrate the vascular phase by assessment of the tracer inflow. The next phase, 5–10 min after injection, known as blood pool phase, consists of image acquisition of tracer distribution of the soft tissues in the region of interest. It reflects tissue distribution of the tracer, especially hyperemia. The next phase consists of delayed images, 3–4 h after injection, when the maximal uptake of the tracer is present. The "whole-body" or "focal static" images are acquired at this time. The three-phase bone scan is indicated in primary bone tumors, trauma, or infectious/inflammatory processes.

Bone scintigraphy is indicated for diagnosis and follow-up of several conditions such as malignancy, infection and inflammatory processes, temporomandibular joint disorder, cystic change, activity of mandibular condyle hyperplasia, and viability of bone grafts.

5.1 Statistics and indications in maxillofacial surgery

Maxilla and mandible are common sites that are affected by neoplasms such as sarcomas and carcinomas. Sarcomas are originated from the mesenchymal part of the jaw. In contrast, the carcinomas can originate either by the locoregional lesions of the oral mucosa or as metastasis of a primary tumor such as adenocarcinomas of the breast, prostate, thyroid, colon, and uterus.

Metastases are the cause of up to 8% of oral malignancies. Due to bone marrow scarcity in the maxilla and mandible, less than 1% of oral malignancies are bone metastases.

In the oral region, etiologies such as osteomyelitis, trauma, and osteoarthritis can also lead to positive bone scans. Chronic osteomyelitis is a challenge especially in the differential diagnosis of the oral and maxillofacial primary cancers [24] (**Figure 1**).

5.2 Bone scintigraphy in osteomyelitis

There are different types of osteomyelitis of the jaw which can be divided into purulent, osteoradionecrosis, and noninfectious (diffuse sclerosing osteomyelitis).

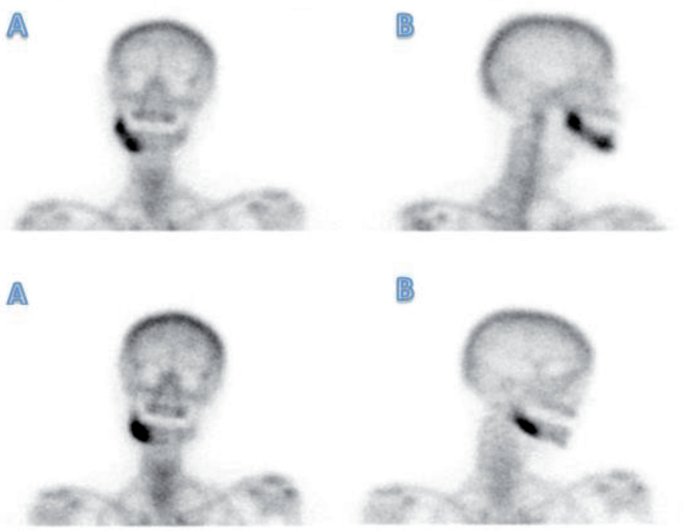

Figure 1.
Bone scintigraphy of a patient with chronic osteomyelitis shows elevated osteoblastic activity as a result of infection in the angle of mandible and mental protuberance of the right jawbone. The lower row of pictures shows the reduction of the involved area after antibiotic therapy and multiple bone curettages. (A) Anterior view and (B) lateral view.

Medication-related osteonecrosis (MRONJ) of the jaw is another subtype of osteomyelitis which is on the rise [25].

MRONJ is a difficult clinical diagnosis in the field of maxillofacial surgery and dentistry. It results from drugs that have anti-bone resorption effects such as denosumab or antiangiogenic medications like sorafenib and also in patients undergoing bisphosphonate therapy. This complication occurs only in the jaw bones. According to some studies, the incidence of MRONJ is around 12%. Due to the rising number of bisphosphonate therapy, over a million prescriptions a year in USA, the exact knowledge of this complication, is essential.

The typical clinical features are painful jaw swelling, loosening of teeth, or extrusion of the jawbone [26–28].

At the early stage of the disease, conservative approach such as pain killers and antibiotics is the treatment of choice, whereas in advanced stages, due to bone exposure, infection, necrosis, and other bone-related complications, surgical intervention such as debridement or resection should be considered [27].

Bone scintigraphy has proved to be a useful diagnostic tool in the early stages of MRONJ. It has the sensitivity of 67% and specificity of 79% in early asymptomatic stages in patients with castration-resistant prostate carcinoma under bisphosphonate therapy [29].

Although several studies show the high detection rate of MRONJ in bone scans, it is still not the routine diagnostic modality in daily practice [30, 31]. However, it should be considered not only for staging or follow-up but also to control the bone status of the jaw (**Figure 2**).

5.3 Bone scintigraphy in fibrous dysplasia

Fibrous dysplasia (FD) is a rare benign lesion in young patients. Fibro-osseous tissue replaces the healthy tissues causing bone overgrowth; sometimes it regresses after adulthood. It could be monostotic (single bone involvement) or polyostotic (more than one bone involvement). Craniofacial bones are mostly prone to be involved. It can be asymptomatic or presents itself with bone malformation,

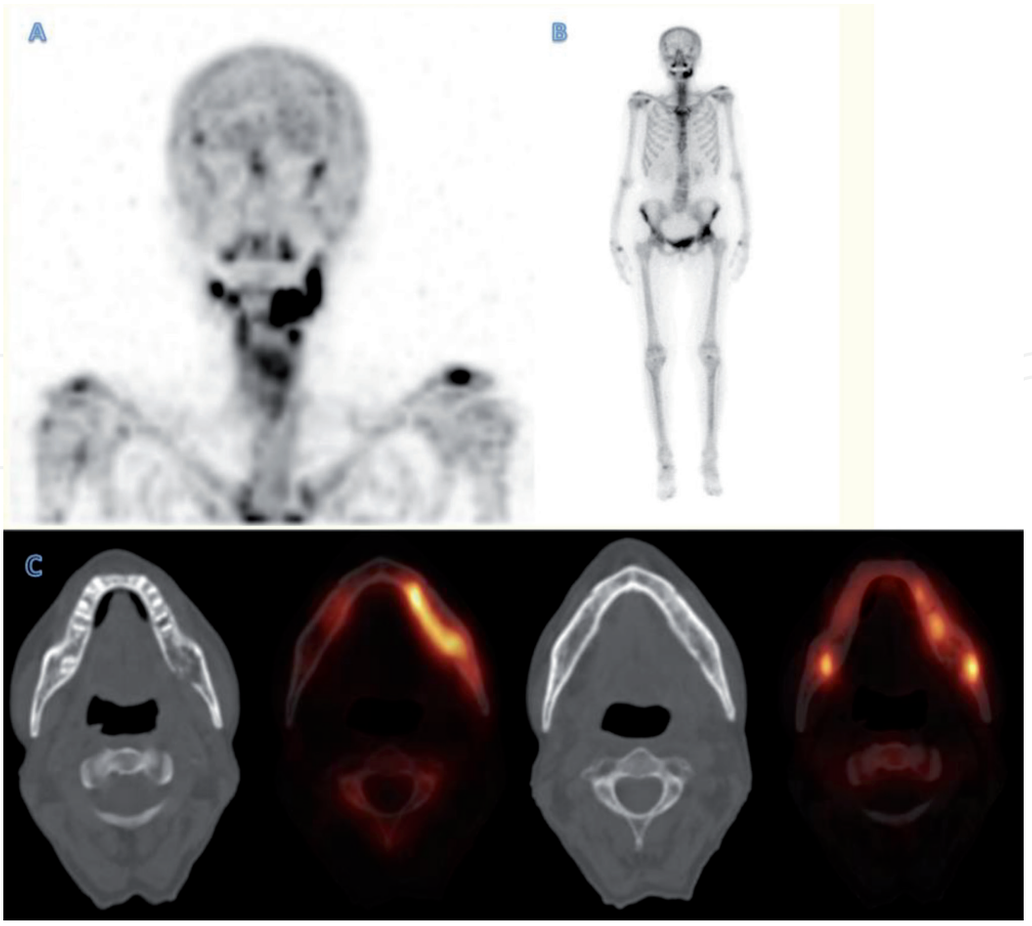

Figure 2.
(A) Bone scintigraphy in a patient after tonsillectomy due to squamous cell carcinoma and chemo radiotherapy with osteonecrosis of the mandible. The osteoblastic activity is visualized in both sides of the mandible. The hot spots show osteoblastic activity in the jaw. (B) Whole-body scan confirms negative bone metastases in the skeleton. (C) SPECT/CT images show the combination of anatomical and biological images.

pain, or pathological fractures. Several studies show the significant technetium 99m-methylene/diethylene diphosphonate (MDP/DPD) uptake on the bone scan.

FD requires long-term medical observation. Surgery is needed when there are signs of bone deformation, pain, compression of the nerve, or malignancy transformation. The probability of malignancy is less than 1%, and it occurs primarily in patients with the history of radiotherapy (**Figure 3**).

Fibrous dysplasia imitates malignancy, especially in patients with previous history of cancer, and can be a difficult differential diagnosis; the exact diagnosis and knowledge of its radiological features can prevent unnecessary workup and possible unnecessary intervention [32].

5.4 Bone scintigraphy and Paget

Single-photon emission tomography/computed tomography (SPECT/CT) is another radionuclide imaging study and is used to visualize three-dimensional multiplanar tracer distribution in the region of interest with CT using an integrated CT scanner [33].

With the aid of SPECT/CT, the exact anatomical location and pathological metabolism can be assessed.

Paget's disease of the bone is a pathological metabolic condition, with abnormal bone resorption. An intense osteoblastic activity is the hallmark of the disease. Some patients are asymptomatic, whereas others present with bone deformity, pain, pathological fractures, osteoarthritis, and rarely neoplasm. Due to high

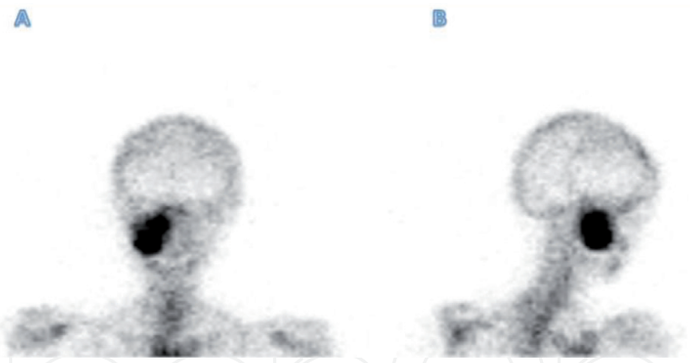

Figure 3.
Bone scintigraphy in a patient with fibrous dysplasia of the right maxilla. It shows the significant high radionuclide uptake, which also may be seen in bone malignancies with high osteoblastic activity. (A) Anterior view and (B) lateral view.

	Bone scintigraphy
Indications	• Specific bone diseases ○ Oncology (e.g., bone tumors and bone dysplasia) ○ Rheumatology (e.g., osteonecrosis of the jaw) ○ Bone and join infection (acute, subacute or chronic osteomyelitis, malignant external otitis) ○ Traumatology and orthopedics ○ Metabolic bone disorders (skeletal manifestation of rare endocrine disorder such as acromegaly and hyperthyroidism) • To investigate unclear symptoms ○ Subacute or chronic musculoskeletal or bone pain with normal clinical examination and radiographs i. Arthralgia, bone pain localized or multifocal ○ As a complementary diagnostic tool in cases of abnormal biological and radiological abnormalities ○ Exclusion of osteomyelitis in case of fever of unknown origin • Metabolic assessment prior to therapy ○ Evaluation of osteoblastic activity before initiating treatment with bisphosphonates
Absolute and relative contraindications	• There is no absolute contraindication. In general, in nuclear medicine, scans are not suitable for pregnant women; the benefit versus risk should be considered and discussed • Breastfeeding should be interrupted for 4 h
Disadvantages	• Low specificity in bone disorders • Limitation of the technique in certain diseases • Not easily accessible
Advantages	• Higher sensitivity in bone disorders • Early detection of bone physiology and pathology

Table 1.
Brief overview of indications, contraindications, advantages, and disadvantages of bone scintigraphy.

osteoblastic activity, significant tracer uptake is visualized on bone scan. In the case of mandibular involvement, it may cause a total involvement of the mandible. In this case, it is called "black beard," which demonstrates the tracer uptake in the entire jawbone.

Unilateral condylar hyperplasia (UCH) is a rare pathological growth of the mandibular condyle, during growth phase in adolescence. Facial asymmetry, malocclusion, deformity, and sometimes pain and temporomandibular joint dysfunction are the common clinical features. Condylar hyperplasia is a self-limiting status; however, due to the unproportioned growth of one condylar, it always results in one-sided facial asymmetry. The growth phase is classified into two phases: active phase and stationary phase. The mandibular asymmetry is highly correlated to the active phase. Routine imaging modalities such as X-rays and CT show anatomical changes. Bone scintigraphy alone or in combination with SPECT can provide both anatomical and functional information, especially in the early stages of the disease before any morphological changes are visible.

Morphological imaging modalities should be used in combination with bone scintigraphy, which provides information on osteoblastic activity. For example, in case of condylar hyperplasia, bone scintigraphy can determine if the growth has stopped before any treatment implemented. Symmetrical uptake in both sides of the jawbone shows no more progression, and therefore treatment can be undertaken.

Early detection of bone physiology and pathology is the greatest advantage of bone scintigraphy, which makes it more sensitive than X-rays. However, its low specificity is its disadvantage. Combining the interpretation of both procedures may decrease their limitations (**Table 1**).

The extension of benign bone lesions such as odontogenic myxoma, keratocyst, and ameloblastoma can be determined by bone scintigraphy. The radionuclide tracer uptake is usually elevated, and the bony changes may be significantly more prominent, compared to X-ray. This information helps the treatment by planning a more extended resection and therefore prevents recurrence.

Bone scintigraphy has its own advantages and disadvantages. It is the responsibility of maxillofacial team to orchestrate imaging modalities in order to decide on the best treatment and to plan follow-up [32].

6. PET/CT scan and oromaxillofacial tumors

As an advanced screening method, PET/CT can detect exact anatomical extension as well as the biological behavior of the tumor.

The fundamental characteristic of human malignancies is the overexpression of the glucose transporter, especially in HNSCC (**Figure 4**).

It can be assessed by high glucose metabolism in the tumors with F18-2-fluoro-2 deoxy-D-glucose (FDG) and PET/CT known as FDG-PET/CT (**Figure 5**).

The combination of PET and CT enables immediate sequential detection of metabolic (FDG-PET) and morphological (CT) information by one examination. Although various methods for retrospective co-registration of PET and CT images have been available since the 1980s, PET/CT imaging has only recently been clinically established through the availability of combined PET/CT (**Table 2**).

In summary PET/CT scan indications are as follows:

a. Differentiating benign from malignant lesions.

b. Search for an unknown primary tumor if metastasis is the first tumor manifestation or if paraneoplastic syndrome is present.

c. Staging of a known tumor condition.

d. Determine response to therapy in the case of known tumors.

e. Assessing the presence of residual tumor disease (vital tumor tissue vs. scar tissue).

f. Determining recurrence, for example, with increasing tumor marker concentration.

g. Selecting exact site for biopsy.

h. Help with radiotherapy planning and non-oncological issues (e.g., infection) [34].

However, it is not yet a gold standard technique according to most guidelines.

Head and neck cancers (HNC) are responsible for approximately 4% of all cancers in the United States. The survival rate in the early stages is up to 80%, whereas in advanced stages, the survival rate can be lower than 40% [35, 36].

Initial assessments of local tumor extension and regional lymph node involvement are of critical importance in head and neck squamous cell carcinoma (HNSCC) and in implementing the most appropriate treatment.

Physical examination, fiber optic endoscopy, CT, and MRI are initial steps to access the local extension of the primary tumor and the regional lymph node status [37]. Recently, positron emission tomography/computed tomography (PET/CT) has found its place in the early workup diagnosis in HNSCC due to its whole-body imaging capability.

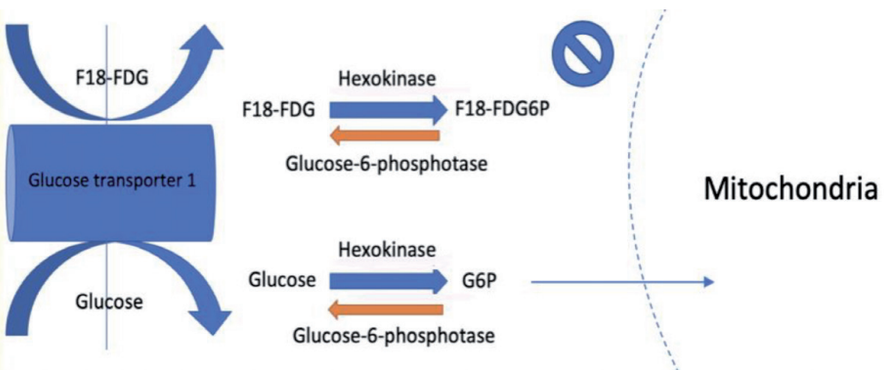

Figure 4.
Schematic of the metabolic trapping of F18-FDG in a tumor cell showing the trapping mechanism in FDG imaging. The glucose transporter 1 (GLUT1) serves as a channel for its uptake. It accumulates in tumor cells, where the metabolism by hexokinase and glucose-6-phosphatase takes place. FDG will be phosphorylated by hexokinase. Glucose-6-phosphotase (G6Pase) counteracts hexokinase phosphorylation by converting glucose-6-phosphate (G6P) to glucose. Therefore, high G6Pase activity leads the accelerated conversion of FDG-6-phosphate (FDG6P) to its FDG form, as a result, the uptake reduces, and it will be released from the cell.

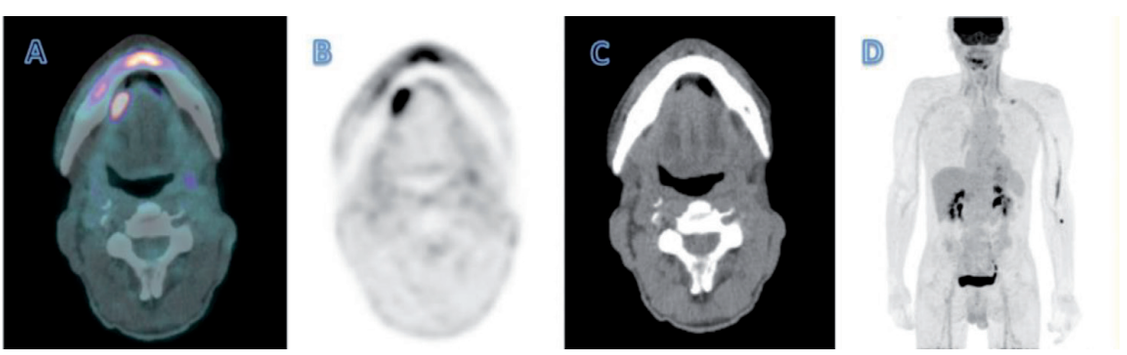

Figure 5.
PET/CT with F18-FDG shows the high metabolism in the lesion in the floor of the mouth, without any local and remote metastasis in stem-body scan. (A) Fusion image, (B) PET, (C) CT, and (D) stem-body scan.

According to different studies, the PET/CT can change the course of pre-treatment, TNM classification, as well as therapeutic management by 31–43% in comparison to conventional workup diagnoses especially in patients with advanced stages of HNSCC (stages III and IV) [37–39] (**Figure 6**).

Thus, its clinical impact is not limited to malignancies of the maxillofacial region. The clinical role of FDG-PET/CT in dental implantology has shown its usefulness in implant monitoring, especially in understanding the implant loss. The most common cause of implant loss is peri-implantitis possibly due to infectious and inflammatory etiologies. Benouaich et al. discussed the relevance of FDG-PET/CT diagnosis in implantology. In their study, they showed that the

PET/CT	
Indications	• Primary diagnostic: unknown primary malignancy, differentiation • Staging pre-treatment and on presentation: nasopharyngeal cancer • Evaluation of the treatment response: • Restaging in case of relapse • Radiotherapy planning of malignant and benign lesions
Absolute and relative contraindications	• There is no absolute contraindication. In general, in nuclear medicine, scans are not suitable for pregnant women; the benefit versus risk should be considered and discussed • Breastfeeding should be interrupted for 4 h
Disadvantages	• No specificity for tumor types • Chances of false positive especially in infection-inflammation • Very small lesion under 5 mm can be missed • Radiation exposure
Advantages	• Several tumors • It provides whole-body imaging, which allows for the exploration of distant metastasis • It has a high resolution • High accuracy because of combined CT images • High sensitivity depending on metabolic activity • Well tolerated

Table 2.
A brief overview of indications, contraindications, advantages, and disadvantages of PET/CT.

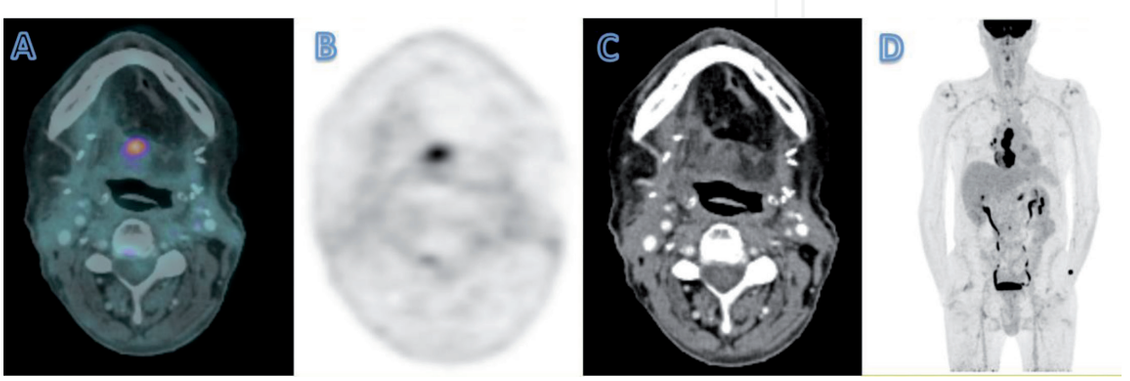

Figure 6.
PET/CT with F18-FDG shows the pathological activity in the residual tongue after partial resection. The stem-body scan demonstrates the hypermetabolic active mediastinal and thoracic lymph nodes as well as a single lumbar bone metastasis. (A) Fusion image, (B) PET, (C) CT, and (D) stem-body scan.

FDG-PET/CT plays an essential role in differentiating normal osseointegration of an implant from peri-implantitis. As a result of the pathological hypermetabolism of the peri-implant, it can be identified by FDG-PET/CT, leading to corresponding treatment [40].

7. Lymphoscintigraphy and sentinel lymph node in oral and maxillofacial surgery

Sentinel lymph node was first described in 1980s when Donald L. Morton, a surgeon at the John Wayne Cancer Center in Santa Monika, and his pathologist Alistair J. Cochran suggested the idea of lymph node mapping with biopsy of the sentinel lymph node in melanoma. They described the sentinel lymph node as the first node, which is the first portal in the diseased cell migration from the lesion. They proposed the importance of the first node on the localization of the lesion. In their paper they emphasized that a "sentinel node" is the initial lymph node upon which the primary tumor drains. Today we know that the sentinel lymph node is the first node on the lymphatic pathway that drains directly from the tumor [41].

SLNB was initially used in melanoma and breast cancer. The indications are melanoma with Breslow thickness up to 1mm, high-risk squamous cell carcinoma, and Merkel carcinoma. Due to the anatomical complexity of the lymphatic pathways in the head and neck region, its importance has been recently appreciated in oncology. To avoid unnecessary neck dissection to decrease the morbidity and improve the patient's quality of life, it is suggested to perform SLNB also in head and neck cancer patients.

Cervical lymph node involvement status is the crucial deciding element in staging, management and predicting prognosis in patients with head and neck SCC.

Recent studies have shown the potential of SLNB as a minimally invasive procedure for assessing occult metastasis and thus reducing morbidity in patients undergoing elective neck dissection (END). Its reliability in T1-T2N0 in the oral cavity and oropharyngeal cancers has been validated for more than a decade, yet till today there is no consensus reached as to when and on whom to perform.

In the field of nuclear medicine, the sentinel lymph node is the first node that is visible after the administration of the tracer. Flow imaging or "dynamic phase" is the first phase, immediately after injection, which shows the lymphatic pathway and clearance. In the late stage also known as the "static phase", can the very first node or sometimes more than one node be visualized and anatomically pinpointed.

Lymphatic mapping is performed with either radiolabeled tracers or vital blue dye (VBD). In conventional lymphoscintigraphy, the main tracer is technetium 99m-labeled radio colloids. The most widely used radiotracer in the United States is technetium 99m-sulfur colloid, and in Europe technetium 99m-albumin-based-nano colloid is used. They both, however, lack optimal rapid clearance of the injection site, high accumulation within the first node, and minimal tracer uptake in the distant nodes [42].

Recently, to overcome the limitations of the conventional colloid tracers, a new tracer has been developed to fulfill the aforementioned shortcomings. Technetium 99m-diethylenetriaminepentaacetic acid (DTPA)-mannosyl-dextran (also known as 99mTc-tilmanocept) is a novel radiopharmaceutical agent that selectively binds to CD206 receptors, which presents in high concentration in lymph nodes on the membrane of macrophages and dendritic cells. Tilmanocept structure consists of a dextran main domain and the DTPA as well as mannose units which are attached to the central part. The average diameter of this macromolecule is 7nm. The mannose binds to the CD206 receptor, whereas the DTPA serves as the binding part for

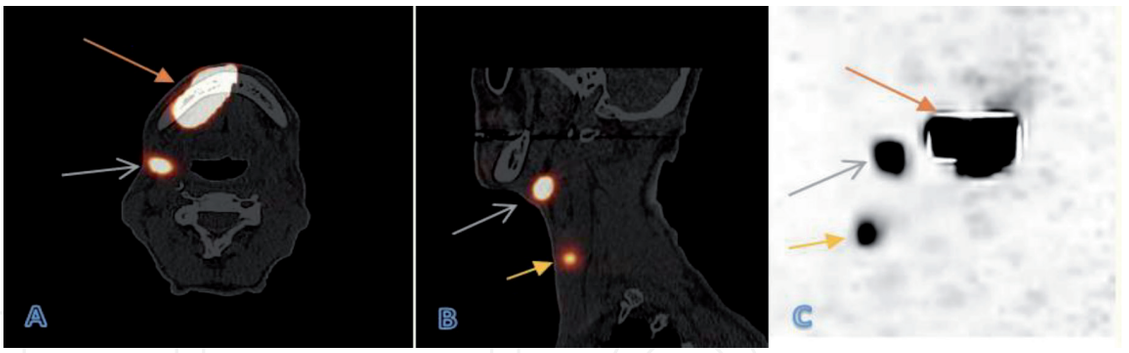

Figure 7.
Sentinel node scintigraphy in a patient with SCC of the soft tissue between the body of mandible and the hyoid bone (orange arrow) and negative clinical examination as well as normal lymph node status in MRI. To avoid radical neck dissection sentinel node scintigraphy has been performed to detect the nodes with direct drainage from the lesion. After 60 min, two cervical lymph nodes were visualized (white and yellow arrows). (A) Axial view, (B) sagittal view, and (C) planar image.

technetium 99m. Due to its small size, it has a rapid uptake in lymph nodes, and its targeted binding prevents its migration to distal nodes [43, 44].

Recent studies have shown the high sensitivity and specificity of up to 94% of tilmanocept in patients with head and neck squamous cell carcinoma [45, 46]. Assessment of single-photon emission computed tomography with computed tomography (SPECT/CT) in addition to planar lymph scintigraphy provides precise anatomical localization in clinically negative nodal status and early stages of the head and neck cancers [24] (**Figure 7**).

8. Conclusion

Diagnosis of cancer and inflammatory diseases and the differentiation between the two are of utmost importance. Nuclear medicine by using radionuclide substances can detect the dynamic aspect of a disease process, and when this dynamic study is mingled by a morphological study, CT or MRI, the management team can see a clearer picture of the disease process and plan treatment protocols accordingly. Sentinel lymph node biopsy is gaining momentum in cancer treatment protocols as a MUST-DO procedure before the definitive treatment plan is implemented.

Conflict of interest

The authors declare no conflict of interest.

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