REVIEW ARTICLE

Nuclear medicine in orofacial diagnosis: A review
Padmashree Shreenivasamurthy1, Sridhar Lakshmana Shastry2

1Department of Oral Medicine and Radiology, Vydehi Institute of Dental Sciences and Research Centre, Bengaluru, Karnataka, India,
2Department of Cardiology, Sri Jayadeva Institute of Cardiovascular Sciences and Research, Bengaluru, Karnataka, India

Abstract
Radionuclide imaging is a form of noninvasive functional imaging technique, which provides information on pathophysiological and pathobiochemical processes. The other special imaging modalities, such as computed tomography (CT), magnetic resonance imaging, and diagnostic ultrasonography, are morphologic imaging techniques. Radionuclide imaging uses radioactive isotopes that emit γ (gamma) rays. Radionuclides allow measurement of tissue function in vivo and provide an early marker of disease, through measurement of biochemical change. After the radionuclides are administered, they get distributed in the body according to their clearance kinetics of that tracer. The gamma camera detects γ-rays and forms planar images showing the locations of the radionuclides in the body. The use of a scintillation crystal for an acquisition of data for image formation has led to the labeling of this technique as scintigraphy. Radionuclide imaging faces a parallel evolutionary shift from imaging function at the organ/tissue level to detecting changes at cellular and molecular levels. Single photon emission CT imaging and positron emission tomography imaging are advanced nuclear medicine techniques. This review provides an overview of the application of modern radionuclide imaging in the diagnosis and management of oral and maxillofacial diseases.

Keywords
Nuclear medicine, positron emission tomography, radionuclide imaging, single photon emission computed tomography

Correspondence
Dr. Padmashree Shreenivasamurthy,
Department of Oral Medicine and Radiology, Vydehi Institute of Dental Sciences and Research Centre, Whitefield, Bengaluru - 560 066, Karnataka, India.
Phone: +91-9448048320.
E-mail: srisrisastry@gmail.com

Received 10 November 2015; Accepted 25 December 2015
doi: 10.15713/ins.jcri.99

Introduction
Nuclear medicine is an independent medical specialty which the World Health Organization has defined as incorporating all applications of radioactive materials in the diagnosis or treatment of the disease, and in medical research. It is mostly an outpatient-led practice which is applicable to many of the diseases and disorders of function that occur in most of the organs of the body including in dental discipline. The diagnostic modalities of nuclear medicine in oral and dental practice should be increasingly considered and an increased awareness for a dental surgeon is needed. These techniques are non-invasive and generally of negligible risk to the patients and do not interfere with their daily activity. Some techniques are specific for particular conditions, whereas others are of more general application. The basis of each nuclear medicine technique is the administration of a very small amount of a chemical agent which is labeled with a tiny amount of a radioactive isotope, a radionuclide, which is called radiopharmaceuticals. They are designed to demonstrate a normal or altered function of the organ, tissue or system for which they are chosen.

Radioisotopes in Nuclear Medicine
Radioisotopes or radionuclides are artificially produced, unstable atoms of a chemical element, which have a different number of neutrons in the nucleus, but the same number of protons and the same chemical properties. Many live for only minutes. Their existence is measured in “half-lives.” That is, the time taken for half of the isotope to disappear.

The radioisotopes have many applications in the field of medicine and dentistry (Table 1). Many applications employ a special technique known as “tracer technique.” A small quantity of a radioisotope is introduced into the body usually by an intravenous injection. After the administration of the radiopharmaceutical, the patient typically lies on a couch. The imaging system - A gamma camera is placed over the relevant part or parts of the body to obtain images of the distribution of the injected radiopharmaceutical. For images of the whole body and or of sections through the body, single photon emission computed tomography (SPECT), may be undertaken. For the latter, the Gamma camera is rotated around the patient to collect such information.
For the selection of radioactive isotopes, the paramount aim is to obtain the desired information with as much certainty and as little irradiation to the patient as possible. To achieve this following are the desirable features of the “tracer material” (though not always entirely attainable).

The “Tracer” substance: This should be as far as possible, be identical in its chemical and biological properties to the stable substance being investigated. The “label”: The “labeling” isotope should remain attached to the “labeled” tracer substance throughout the investigation.[6,4]

Generators for short-lived isotopes include tellurium 132 which has a half-life of 78 h and has iodine 132, its daughter product, which has a half-life of 2-3 h. Similarly, technetium 99 m (6 h), indium 113 m (1.7 h), and strontium 87 m (2.8 h) are, respectively, decay products of molybdenum 99 (67 h), tin 113 (118 days), and yttrium 87 (80 h). The most commonly used is technetium 99m ($^{99m}$Tc). In each case, the daughter is chemically different from the parent and can be separated from it chemically. This is the basis of the “generators” (or “cows” as they are often called) which can provide supplies of short-lived isotopes over a period of days. In practice, the column (or “cow”) is eluted (or “milked”) daily over about a week, after which time it becomes weak, the activity of the tellurium being down to about one-quarter of its original value.[6-8]

Gamma Camera

Gamma cameras (also called anger cameras and scintillation cameras) are the most common means of forming an image. These cameras capture photons and convert them to light and then to a voltage signal. This signal is reconstructed to a planar image that shows the distribution of the radionuclide in the patient. Gamma camera consists of different components such as collimator, scintillator, and photomultiplier tubes.[9]

Emission Tomography

SPECT

The SPECT technique is particularly valuable because of its unique ability to locate the precise location of an abnormality from the three dimensional image it produces. This SPECT technique uses a gamma camera to record images at a series of angles around the patient.[10]

Positron emission tomography (PET)

When we administer a positron-emitting radionuclide to a patient, the emitted gamma rays, can be detected by a radiation detector surrounding the patient. The tomographic images are then generated using a computer which has anatomic accuracy.[1,11]

18F-fluorodeoxyglucose (FDG) is a radiopharmaceutical commonly used for studying glucose use in brain, heart and to look for cancer metastasis.[12] In the first stages of normal glucose pathway the living cells take up FDG, an analog of glucose. Since the cancer cells have increased glycolytic activity, the FDG is trapped into these cancer cells. This is the main reason behind the use of FDG as a tracer. The renal system helps in the excretion of this FDG as the reabsorption of the tracer is not possible. Therefore, FDG-PET can reveal the presence of a tumor when conventional morphological diagnostic modalities such as X-ray, CT, magnetic resonance imaging (MRI) and ultrasound do not yet detect any evident lesions. It is becoming more and more widespread for the diagnostic assessment of patients with suspected malignancies, in tumor staging, and in monitoring therapy.[13,14]

Role of Nuclear Medicine in Dentistry

Nuclear medicine has become an advanced diagnostic procedure in all fields of medicine. Advanced procedures such as SPECT and PET, hold lot of promise in all diagnostic areas, including dental arena. However, it is relatively poorly understood with respect to dental applications and in oral and maxillofacial pathologies it is underutilized. Its application in diagnostic as well as therapeutic fields of oral/maxillofacial pathologies needs discussion and emphasis.[15]

A dental care provider may utilize the diagnostic isotopes to study the head and neck tumors, salivary gland diseases, and many metabolic diseases and infectious processes. Even before morphological changes are evident in the tissue, the abnormalities can be promptly detected by these radionuclide scans.[15]

Bone imaging techniques

Conventional and digital radiographs remain the most easily available tool for the detection of diseases of teeth and bones of the oral cavity. Sometimes early detection of these jaw lesions becomes more difficult because they do not develop physical symptoms at an early stage when biochemical changes are taking place. The bone scan can show these early changes in the osteoblastic activity which would not appear on the radiographic images. Although the resolution of bone scintigraphy is not as good as that of radiographs, it can even detect approximately a 10% increase in the osteoblastic activity of the bone above normal.[16]

Standard bone scan, three phase bone scan and SPECT are the bone imaging techniques. The static images acquired by these scans are generally taken after 3 h - As delayed static images are useful in the evaluation of benign conditions (condylar hyperplasia). There is increase in the new bone formation with the bony lesions which have the highest morbidity. These areas of new bone formation can be detected by scintigraphy as there is increased uptake of the radiotracer known as "hot spots."[16]

Bone imaging techniques can be utilized to diagnose various disease processes in dentistry:

Inflammatory and infectious processes

A positive bone scan image is seen in inflammatory conditions such as osteomyelitis, osteoarthritis, traumatic injuries, periapical lesions and periodontal lesions.[16]
Fibrous dysplasia
Fibrous dysplasia of bone may be monoosteotic (jaw bone) or polyosteotic. There is a slow and insidious enlargement of bone which may persist until growth cessation or continue to adulthood. Nuclear medicine demonstrates increased tracer uptake on 99mTc bone scans.

Paget disease
In Paget’s disease, there is abnormal resorption and apposition of bone in one or more bones. The disease is initiated by an intense osteolytic activity with resorption of normal bone followed by a vigorous osteoblastic activity forming woven bone. In addition to radiographs an increased uptake of radiotracer by scintigraphy demonstrates these lesions. When the mandible is affected, the bone scan may demonstrate marked uptake throughout the entire mandible from condyle to condyle, a feature that has been termed black beard or Lincoln’s Sign. 

Fracture
Most fractures show increased uptake on bone scintigraphy within hours after trauma. In elderly patients, however, fractures may take several days to be seen on bone scan. The optimal timing for imaging of a fracture is unclear. Holder et al. reported a sensitivity of 93% and specificity of 95% for fracture identification if the bone scan is performed within 72 h and 100% sensitivity if performed 72 h or longer after injury. In addition to patient’s age, the bone metabolic activity, mineral content, and imaging technique are all factors that can significantly affect the ability to detect a fracture. The scintigraphic appearance of fractures depends on the time elapsed since injury.

Condylar hyperplasia
Condylar hyperplasia of the mandible is a pathologic state of development that can lead to facial asymmetry, mandibular deviation, malocclusion, and articular dysfunction. This abnormality is important in dentistry due to induction of lateral open bite, midline shift, prognathism, temporomandibular joint dysfunction, and malocclusion. Bone scintigraphy has been used in the diagnosis and treatment planning of mandibular condylar hyperplasia for many years. This imaging modality has the ability to detect abnormalities at an earlier stage before morphological changes are evident.

Gallium 67-citrate imaging
After the administration of the gallium 67-citrate intravenously, it gets accumulated in the areas of inflammation, infection and neoplasm, non-specifically. A gallium scan is used in the evaluation of abscesses, osteomyelitis, and lymphomas. Although not a favorite test, suspicion of osteomyelitis in dental and other areas can be confirmed and diagnosed effectively by gallium scan. Although triple phase bone scan test is the choice for osteomyelitis, it is non-specific and gallium imaging increases the specificity of positive bone scan. Gallium scan is also used to monitor treatment response with reduced gallium intake/accumulation indicating improvements in osteomyelitis.

Salivary gland scintigraphy
The use of a scintillation crystal for acquisition of data for image. Formation has led to the labeling of this technique as scintigraphy. Several modalities are known for salivary gland imaging such as sonography, sialography, scintigraphy, CT and MRI. CT and MRI are well-established in oncological settings because of their high geometric resolution and their well-known differentiation of soft tissue from osseous structures. The parenchymal and excretory function of salivary glands can be simultaneously quantified by salivary gland scintigraphy. Moreover, this method is well-tolerated by the patient, reproducible and easy to perform. Radioactive substance with affinity to particular tissue is administered with radioactivity measured by scintillation camera. The intact salivary gland parenchyma shows the uptake of 99mTc-pertechnetate. Gland aplasia/agenesis, obstruction, trauma, as well as fistulas in the glands can be detected, though there are exceptions. Further, acute inflammation usually shows increase in uptake while decrease intake is seen chronic inflammatory stages.

Lymph node scintigraphy
The sentinel node is the one which first receives lymph the primary tumor. A radionuclide is used in the radioisotope method for sentinel lymph node mapping. Lymphoscintigraphy and gamma probe are used to detect the sentinel lymph node.

Uses of Radio Isotope in Head and Neck Cancer
The oncologic imaging modalities aids in the detection of cancer, it’s staging and in the assessment of prognosis. 18F-FDG PET has a significant in the diagnosis and management of head and neck cancer. It helps in the detection of distant metastasis. The possibilities of distant metastasis increase with locally advanced diseases (T3-T4), regional lymph node involvement (N2 or N3) with extracapsular involvement, and perineural invasion. Chemoradiotherapy has a significant role in the treatment of head and neck cancer. Being a modality to assess the metabolic activity of the malignant cells, 18F-FDG PET plays a major role in detecting response to the treatment.

Uses of Radioisotopes in Brachytherapy
Brachytherapy is one of the radio-therapeutic methods where the radioisotopes are directly placed at the site of the malignant tumor. These isotopes are placed in a protective capsule which prevents its movement and later the capsule may be left behind or removed. These isotopes emit ionizing radiation to the surrounding tissue and kills the cancer cells.
Advantages of nuclear medicine

- These imaging modalities give the information on primarily displaying the structure of the human body and thereby provide anatomical information that can be used for diagnosis of diseases.
- Nuclear medicine imaging is based on tracer principles and primarily gives images of function, including physiology, biochemistry or metabolism, by analyzing the dynamic behavior of molecules in organs and tissues at different levels.
- Useful for early diagnosis of disease and for evaluation of treatment effects in the early post-therapeutic stage.
- Allows easy demonstration of whole body images and interactive display, which help in detecting the metastatic activity.
- Detailed examinations can be performed on different sites and at different times after the injection of the tracer isotope to clarify findings without increasing radiation exposure unlike other basic techniques wherein number of exposures are performed.

Table 1: Radioisotopes used in nuclear medicine

<table>
<thead>
<tr>
<th>Radioisotopes</th>
<th>Uses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reactor radioisotopes</td>
<td></td>
</tr>
<tr>
<td>Technetium-99 m</td>
<td>To image the skeleton and heart muscle in particular, but is also used for brain and thyroid imaging</td>
</tr>
<tr>
<td>Cobalt-60</td>
<td>For external beam radiotherapy and used for sterilizing</td>
</tr>
<tr>
<td>Iodine-125</td>
<td>In cancer brachytherapy</td>
</tr>
<tr>
<td>Iodine-131</td>
<td>Used in imaging the thyroid function and thyroid cancer treatment</td>
</tr>
<tr>
<td>Iridium-192</td>
<td>Acts as source in internal radiotherapy for cancer treatment</td>
</tr>
<tr>
<td>Molybdenum-99</td>
<td>Used to produce technetium-99 m</td>
</tr>
<tr>
<td>Palladium-103</td>
<td>For brachytherapy in cases where early stage of cancers are detected</td>
</tr>
<tr>
<td>Strontium-89</td>
<td>For pain relief in osteochondromas</td>
</tr>
<tr>
<td>Caesium, gold and ruthenium</td>
<td>As a treatment modality</td>
</tr>
<tr>
<td>Cyclotron radioisotopes</td>
<td></td>
</tr>
<tr>
<td>Carbon-11, nitrogen-13, oxygen-15, fluorine-18</td>
<td>Used in PET scans through use of F-18 in FDG which help to detect, diagnose and know the prognosis of a tumor</td>
</tr>
<tr>
<td>Cobalt-57</td>
<td>Can be used as a detector for hypertrophy of cells, which indirectly determine the division and progression of cell growth to a stimuli</td>
</tr>
<tr>
<td>Copper-64</td>
<td>Is being used in PET scans and to check for the metabolism of copper</td>
</tr>
<tr>
<td>Copper-67</td>
<td>Used as an isotope for radiotherapy</td>
</tr>
<tr>
<td>Fluorine-18 as FLT (fluorothymidine), F-miso (fluoromisonidazole), 18F- choline</td>
<td>Used as traces, in radiotherapy</td>
</tr>
<tr>
<td>Gallium-67</td>
<td>For imaging of tumor size</td>
</tr>
<tr>
<td>Gallium-68</td>
<td>Used in PET scan to detect the metastatic activity</td>
</tr>
<tr>
<td>Germanium-68</td>
<td>Used to generate Ga</td>
</tr>
<tr>
<td>Rubidium-82</td>
<td>Used in PET scan to detect the cardiac myopathies</td>
</tr>
<tr>
<td>Strontium-82</td>
<td>Used to generate Rb-82</td>
</tr>
</tbody>
</table>

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

Disadvantages of nuclear medicine

- Although contrast of a lesion versus surrounding tissues is high when radiotracers accumulate in the lesion, spatial resolution, in general, is poor compared with radiographs, CT or MRI.
- The cost of instruments used is relatively high.
- The cost of each examination also depends on the cost of radiopharmaceuticals used and the capability of the scanner.
- Patients are exposed to ionizing radiation administered to the bodies.
- The radiation exposures are different from radiographs and CT, which involve external and generally only partial body exposure, whereas radionuclide administered into patients causes internal whole body exposure in a non-uniform manner determined by the bio distribution and clearance kinetics of that tracer.
- Due to unavoidable high irradiation from PET tracers to the staff members when interacting with radioactive patients, it is recommended that a 6 mm thick lead shielding is advisable.

Conclusion

Radionuclide imaging is a patient-friendly, non-invasive technique for detecting various diseases processes in dentistry. It includes techniques which are sensitive and specific for imaging inflammation, infection, and malignancies. It is able to deliver objective measurements before and after intervention, surgery or any other treatment modalities so that outcome analysis can be performed quantitatively. Interpretation of the scan results, as well as the pitfalls involved is important to understand, as they may be required at times to be done by the dental surgeons. Bone scan, SPECT imaging and PET scans are the techniques that help in diagnosing oral/dental pathologies and tumors. In the present era, since nuclear diagnostic techniques are being used commonly in dental practice, it is important for the dentists to be familiar with these scans in nuclear medicine and also to be well versed with the various indications for nuclear imaging techniques in oral/dental pathologies.
References