Review Article

Nuclear medicine in dentistry revisited: New avenues to explore

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ABSTRACT

Nuclear medicine and radioactive tracers have considerable application in dental research, because they provide one of the few practical methods for studying the limited metabolic activities of bones and teeth. The ease with which minute amounts of these radioactive materials may be accurately measured and distinguished from the mass of inert element in the tooth is particularly valuable. They are useful in studying many problems of calcification and mineral exchange. There are also opportunities of their use in investigating fluorosis, caries protection, periodontal disease, micro leakage studies of dental materials, root resorption, nutritional, and endocrine effects, as well as numerous other dental problems. Other usages of nuclear medicine in dentistry are listed below: Age written in teeth by nuclear tests, scintigraphic evaluation of osteoblastic activity, and evaluation of osteoblastic activity around dental implants using bone scintigraphy. Nuclear medicine can be an indicator of "active" alveolar bone loss. Nuclear medicine techniques are used as an adjunct for the diagnosis of oral diseases (benign tumors and carcinomas) and temporomandibular joint disease. This review article discusses these indications of nuclear medicine.

Key words: Alveolar bone loss, nuclear medicine, oral disease, osteoblastic activity, radionucleotides, scintigraphy

INTRODUCTION

Nuclear medicine is a branch or specialty of medicine and medical imaging that uses radionuclides and relies on the process of radioactive decay in the diagnosis and treatment of disease.[1]

Nuclear medicine field uses non-hazardous, painless, and economical techniques to image the body and treat the disease. Nuclear medicine imaging gives us information about both structure and function.[1] Medical history of many diseases that may require surgery or necessitate more expensive diagnostic tests can use nuclear medicine method for their diagnosis.[1] Nuclear medicine imaging procedures often identify abnormalities very early in the progress of a disease long before many medical problems are apparent with other diagnostic tests.

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Nuclear medicine uses very small amounts of radioactive materials (radiopharmaceuticals) to diagnose and treat disease.[1] In imaging, the radiopharmaceuticals are detected by special types of cameras that work with computers to provide precise pictures about the area of the body being imaged. In treatment, the radiopharmaceuticals go directly to the organ being treated [Figure 1].

The amount of radiation in a typical nuclear imaging procedure is comparable with that received during a diagnostic X-ray, and the amount received in a typical treatment procedure is kept within safe limits. New and innovative nuclear medicine treatments that target and pinpoint molecular levels within the body are revolutionizing our understanding of and approach of a range of diseases and conditions.[2]

In a nuclear medicine test, small amounts of radiopharmaceuticals are introduced into the body by injection, swallowing, or inhalation. Radiopharmaceuticals are substances that are attracted to specific organs, bones, or tissues.[2] The amount of radiopharmaceutical used is carefully selected to provide the least amount of radiation exposure to the patient, but ensure an accurate test. A special camera [first positron emission tomography scanner (PET), single photon emission computed tomography (SPECT), or

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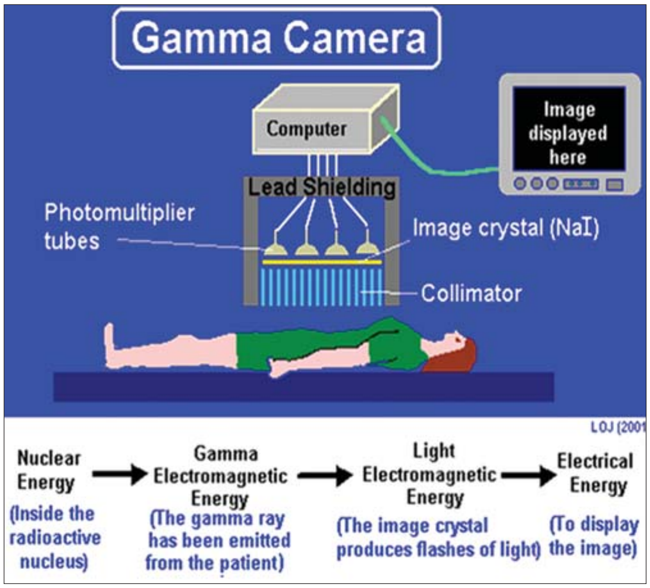

Figure 1: Principle of gamma camera

gamma camera] is then used to take pictures of the body. The camera detects the radiopharmaceutical in the organ, bone, or tissue and forms images that provide data and information about the area in question.[2] Nuclear medicine differs from an X-ray, ultrasound, or other diagnostic test because it determines the presence of disease based on biological changes rather than changes in anatomy. Nuclear medicine procedures are among the safest diagnostic imaging exams available.[2]

To obtain diagnostic information, a patient is given a very small amount of a radiopharmaceutical. Because such a small amount is used, the amount of radiation received from a nuclear medicine procedure is comparable to, or often many times less than, that of a diagnostic X-ray. Most nuclear medicine procedures expose patients to about the same amount of radiation as they receive in a few months of normal living.[2]

HISTORY OF NUCLEAR MEDICINE

The history of nuclear medicine is rich with contributions from gifted scientists across different disciplines in physics, chemistry, engineering, and medicine. The multidisciplinary nature of nuclear medicine makes it difficult for medical historians to determine the birth date of nuclear medicine. This can probably be best placed between the discovery of artificial radioactivity in 1934 and the production of radionuclides by Oak Ridge National Laboratory for medicine related use in 1946.[3]

Many historians consider the discovery of artificially produced radionuclides by Frédéric Joliot-Curie and Irène Joliot-Curie in 1934 as the most significant milestone in nuclear medicine.[3] In February 1934, they reported the first artificial production of radioactive material in the journal *Nature* after discovering radioactivity in aluminum foil that was irradiated with a polonium preparation. Their work built upon earlier discoveries by Wilhelm Konrad Roentgen for X-ray, Henri Becquerel for radioactive uranium salts, and Marie Curie for radioactive thorium, polonium, and coining the term "radioactivity." Taro Takemi studied the application of nuclear physics to medicine in the 1930s. The history of nuclear medicine will not be complete without mentioning these early pioneers.[3]

Nuclear medicine gained public recognition as a potential specialty on December 7, 1946 when an article that described successful treatment of a patient with thyroid cancer metastases using radioiodine (I-131) was published in the Journal of the American Medical *Association* by Sam Seidlin. This is considered by many historians as the most important article ever published in nuclear medicine.[4] Although, the earliest use of I-131 was devoted to therapy of thyroid cancer, its use was later expanded to include imaging of the thyroid gland, quantification of the thyroid function, and therapy for hyperthyroidism.

Pioneering works by Benedict Cassen in developing the first rectilinear scanner and Hal O. Anger's scintillation camera (Anger camera) broadened the young discipline of nuclear medicine into a full-fledged medical imaging specialty.[5]

In these years of nuclear medicine, the growth was phenomenal. The Society of Nuclear Medicine was formed in 1954 in Spokane, Washington, USA. In 1960, the Society began publication of the Journal of Nuclear Medicine, the premier scientific journal for the discipline in America.[5]

Among many radionuclides that were discovered for medical use, none were as important as the discovery and 1937 by C. Perrier and E. Segre. Today, Technetium-99 m is the most utilized element in nuclear medicine and is employed in a wide variety of nuclear medicine imaging studies.[3]

In the 1980s, radiopharmaceuticals were designed for use in diagnosis of heart disease. The development of SPECT, at around the same time, led to three-dimensional reconstruction of the heart and establishment of the field of nuclear cardiology.[5]

More recent developments in nuclear medicine include the invention of the PET. PET/CT imaging is now an integral part of oncology for diagnosis, staging, and treatment monitoring.[5]

NUCLEAR MEDICINE IN MEDICAL FIELD[5]

Many different types of nuclear medicine procedure are used on a routine basis, including the following:

1. Bone scans to evaluate orthopedic injuries, fractures, tumors, or unexplained bone pain
2. Heart scans to identify normal or abnormal blood flow to the heart muscle, measure heart function, or determine the existence or extent of damage to the heart tissues after a heart attack episode
3. Thyroid iodine scans to analyze the thyroid function and show the structure of the gland. Larger doses of radioactive iodine are used to destroy thyroid nodules in case of Graves' syndrome
4. Gallbladder or hepatobiliary scans to evaluate both liver as well as gallbladder function. This test can determine obstructions caused by the presence of gallstones
5. Lung scans to evaluate the flow of blood and movements into and out of the lungs, as well as the determination of the presence of blood clots
6. Gallium scans to evaluate infection and certain types of tumors
7. Brain scans
8. Gastrointestinal bleeding scans.

The most commonly used intravenous radionuclides are shown in Figure 2 and Table 1.

NUCLEAR MEDICINE IN DENTISTRY

Nuclear medicine techniques for the detection of active alveolar bone loss

Bone is a dynamic tissue in which the net balance between formation and resorption determines the final osseous architecture. Tests for periodontal disease activity need to take the dynamic nature of bone into account if activity is to be determined in a single examination. Most tests used to assess the progression of periodontal disease, such as radiography, are capable of detecting changes in the osseous architecture only after it has occurred, because a single examination represents the sum total of all past disease exacerbations and remissions.[6,7] Thus, in order to detect "active" progression of alveolar bone loss by radiographs, two or more examinations must be taken, separated in time. Comparison of the two radiographic images will indicate if alveolar bone loss has progressed during the study period. A test that can detect periodontal disease activity at the time of its occurrence would be capable of indicating active periodontal disease prior to the time the bone loss is evident on radiographs.[6]

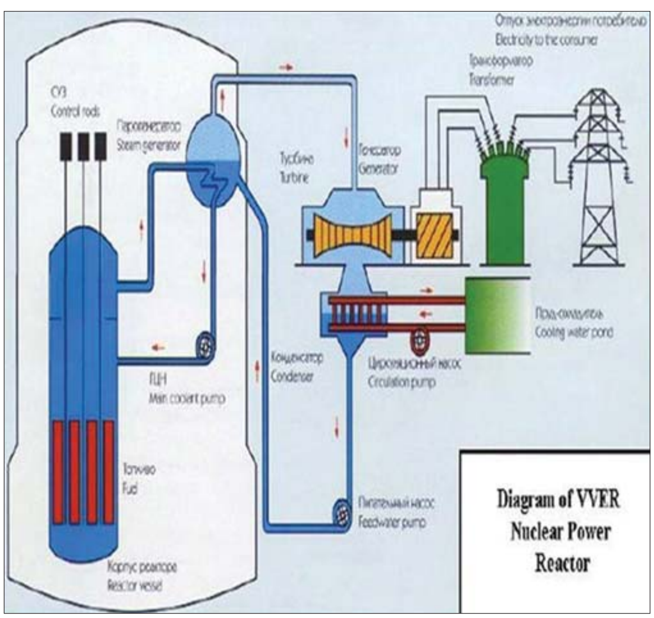

Figure 2: How nucleotide works

The principles of nuclear medicine techniques, which address alterations in bone metabolism, have the potential to detect areas of progressive bone loss in a single examination.[8-11]

Nuclear medicine techniques for the study of bone metabolism, colloquially termed "bone scanning," utilize a radio-labeled bone-seeking radiopharmaceutical. The label 99 m-technetium is a short-lived element with a 6-h physical half-life. Technetium is characterized by its ability to complex with carrier agents and create tissue-specific radiopharmaceuticals.[12,13] In the case of bone, the technetium label is complexed with tin and a diphosphonate moiety, which gives the resultant radiopharmaceutical its bone-seeking quality.[12] In general, the bone-seeking radiopharmaceutical is taken up in the calcifying front of forming bone.[12,14] Uptake may involve complex formation with the mineralized components of bone such as calcium. Since bone resorption is usually coupled with formation behind the resorbing front, nuclear medicine is used to detect alterations in bone metabolism in diseases of bone resorption as well as formation. In medicine, bone seeking radiopharmaceutical uptake (BSRU) is routinely used to detect osseous abnormalities prior to the time of radiographic evidence

Table 1: Common intravenous radionuclides

Radioisotope	Radio gases/aerosol
Technetium-99 m	Xenon-133
Iodine-123 and 131	Krypton-81 m
Thallium-201	Technetium-99m Technegas a radioaeorsol invented in Australia by Dr Bill Burch and Dr Richard Fawdry
Gallium-67	Technetium-99 m DTPA
Fluorine-18	
Fluorodeoxyglucose	
Indium-111 Labeled Leukocytes	

of disease. Nuclear medicine is an early indicator of bony metastases, primary bone tumors, infections, metabolic bone disease, and stress fractures.[13,15,16] In dentistry, nuclear medicine has been demonstrated to be of value in the early detection of periapical pathology[17] and growth disorders.[18-20]

Since periodontal disease is a disease of bone, Jeffcoat *et al*., in 1987[6] developed the hypothesis that a single measurement of bone-seeking radiopharmaceutical uptake is indicative of the rate of bone loss that is equivalent to measurements by sequential radiographic examinations.[8,21]

Jeffcoat *et al*.,[6] performed early studies in the beagle dog model of naturally occurring periodontal disease, and transferred the technology to human subjects. They developed a diagnostic test for periodontal disease activity after the early tests they conducted in the beagle model for naturally occurring periodontal disease and through their preliminary tests in human subjects, indicating that low uptake ratios of the nucleotide are associated with little or no progression of alveolar bone loss and high uptake ratios are associated with bone loss. Since the BSRU measurement is performed in a single visit, the nuclear medicine test has the potential to identify progressive bone loss prior to the time additional bony destruction has occurred and become visible in sequential radiographs. Uptake measurements for the above series of experiments were taken with a miniaturized cadmium telluride probe radiation detector. This instrument displayed "counts detected" and provided a quantitative measure of uptake at each tooth site.[6]

Earlier bone-seeking radiopharmaceuticals, such as 99 m-Tc-Sn-EHDP, used in the first animal study, required a long, 4-h waiting period prior to the imaging process. The radiopharmaceutical, 99 m-Tc-MDP, used in subsequent studies is cleared more rapidly, and uptake may be measured from 1 to 2 h after injection.[6]

Nuclear medicine examinations of bone are now routine in medicine for the detection of non-life threatening diseases. The nuclear medicine examination delivers a radiation dose of approximately 0.5 rem. This dose is routinely used for the detection of stress fractures, frequently observed in healthy patients who jog.[6]

Nuclear medicine and implant dentistry

It is well known that the success or the failure of implants interfaced with bone depends, taking into account a favorable biological reaction, on the structural condition of the biomechanical system constituted by the bone structure and the implant. Knowledge of the strain/stress pattern can allow one to establish if bone maintenance, resorption, or addition is more likely to take place. In the work conducted by Bignardi *et al*.,[22] two different kinds of implant supports for overdenture retention were compared by means of fine element method (FEM), and clinical follow-up was assessed by means of technetium 99m-MDP scintigraphy. The results showed that nuclear medicine technique was comparable to the FEM to evaluate the osteoblastic activity at the implant-bone interface.[22]

Several recent medical reports have focused attention on the possible application of skeletal scintigraphy imaging in odontostomatology. A study was conducted by Bambini *et al*.,[23] which aimed to assess the influence of immediate prosthetic loading on peri-implant osteoblastic activity through bone scintigraphy. They found that Routine planar methodology provided a direct measure of cellular activity of the examined areas.

In spite of the small number of involved patients, the results obtained from this pilot study suggest that nuclear medicine may hold possible advantages in implant dentistry for those who seek to clarify the still unknown aspects of osteoblastic activity.[23,24]

Nuclear medicine and grafts

The study conducted by Berding *et al*.,[25] concluded that [18F-] PET (fluoride ion and positron emission tomography) depicted increased blood flow activity in onlay grafts and regions of osteosyntheses, indicating bone repair in the graft and adjacent host bone early after surgery. For the regions of osteosyntheses, the decrease in both parameters corresponded to uncomplicated healing. The lack of increased influx, although flow was increased in pedicle grafts, most likely indicates that some necrosis occurred in these grafts despite patency of anastomoses. It may be concluded that [18F-] PET provides further insight into the biology of graft incorporation.[25] There are other studies that show that bone scintigraphy performed within the first week after the mandibular reconstruction is a useful tool to monitor the viability and early complications of microvascularized fibular grafts and plays an important role in the decision-making process during repeated surgical exploration. SPECT is more sensitive than planar imaging for assessing graft viability.[26]

Nuclear medicine for oral and maxillofacial regions

The main radionuclide for diseases in the oral and maxillofacial regions are Technetium-99m pertechnetate for diagnosis of tumors in the salivary glands, Gallium-67 for detection of osteomyelitis in the maxilla and mandible, and fluorine-18-labeled fluoro-2-deoxy-D-glucose (F-18-FDG) for detection of malignant tumors in the oral and maxillofacial regions.[27]

F-18-FDG is the most commonly used radioisotope for differentiating benign and malignant disease, in primary tumor staging, and in evaluation of treatment response, recurrence detection, and restaging.[27]

Tmj imaging[28,29]

Scintigraphy aids to discover early changes in the TMJ skeleton that may also result in joint disc abnormalities. Radionuclide 99mTc is used for the examination.

The temporo-mandibular joint is ideal for SPECT, because it is a quite small joint situated close to the skull base and paranasal sinuses. Therefore, SPECT can, unlike the double-dimension featuring, present TMJ separately from the parts of high bone density. The radionuclide examination sensitivity is high, however, its specificity is low. Any inflammation, trauma, or tumors increase the local isotope concentration. For this reason, many studies state that radionuclide examination is relevant only as a screening method.[28,29]

In forensics to determine the age of the teeth[30]

Establishing the age at death of individuals is an important step in their identification and can be done with high precision up to adolescence by analysis of dentition, but it is more difficult in adults. The amount of radiocarbon present in tooth enamel as a result of nuclear testing is a remarkably accurate indicator of when a person was born. Age is determined to within 1.6 years, whereas the commonly used morphological evaluation of skeletal remains and tooth wear is sensitive to within 5-10 years in adults.[30]

DISADVANTAGES

The main drawback of nuclear medicine is the cost of the tests and the equipments used. The foremost hazard to these nuclear tests is radiation exposure. According to the Radiological Society of North America, the dose is low enough to keep the risks small, and the scans have produced no observed long-term effects. But radiation builds up in a patient's body over a lifetime, meaning that patients who undergo many such scans face a higher risk of the negative health effects associated with radiation exposure, such as cancer. There also could be occupational hazards for the technician operating the equipment. Nuclear medicine produces radioactive waste products, creating a disposal problem. Although technicians inject much of the radioactive material into patients, unusable material must be stored permanently where people will not be exposed to it, so regular landfills are inappropriate. A rare complication could be allergic reactions to the radionucliotides used.[31]

CONCLUSION

Imaging with bone-seeking nuclear medicine radiopharmaceuticals has changed dramatically in a span of past 10 years. The only indication for bone scintigraphy a decade ago was to detect skeletal metastases in patients with known carcinoma. Improvements in equipment and radiopharmaceuticals have led to a wide array of uses of nuclear medicine like studies for the detection and evaluation of a multitude of benign abnormalities, osteoblastic activity around implants, and alveolar bone loss in periodontal diseases. Now-a-days, radionucliotides are used to detect traumatic processes involving the skeletal system, connective tissues, and muscles. The literature survey reveals that bone scintigraphy with Technetium-99 m-labeled diphosphonates is one of the most frequently performed of all radionuclide procedures. Radionuclide bone imaging is not specific, but its excellent sensitivity makes it useful in screening many pathologic conditions. Moreover, some conditions that are not clearly depicted on anatomic images can be diagnosed with bone scintigraphy. Bone metastases usually appear as multiple foci of increased activity, although they occasionally manifest as areas of decreased uptake.[32]

Traumatic processes can often be detected, even when radiographic findings are negative. Most fractures are scintigraphically detectable within 24 h, although in elderly patients with osteopenia, further imaging at a later time is sometimes indicated.[32]

A combination of focal hyperperfusion, focal hyperemia, and focally increased bone uptake is virtually diagnostic for osteomyelitis in patients with non-violated bone. Bone scintigraphy is also useful for evaluating disease extent in Paget disease and for localizing avascular necrosis in patients with negative radiographs.[32]

CLINICAL SIGNIFICANCE

Nuclear medicine imaging techniques can be evolved as a routine diagnostic method to evaluate the osteoblastic activity around implants and in periodontal disease, evaluate fractures, benign and metastatic tumors, grafts, and TMJ disorders at an early stage, and thus bring about an intervention therapy.

In the future, nuclear medicine may be known as nano medicine. As our understanding of biological processes in the cells of living organism expands, specific probes can be developed to allow visualization, characterization, and quantification of biologic processes at the cellular and subcellular levels. Nuclear medicine is an ideal specialty to adapt to the new discipline of molecular medicine, because of its emphasis on function and its utilization of imaging agents that are specific for a particular disease process. Radionuclide bone imaging will likely remain a popular and important imaging modality for years to come.

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