Bone Scintigraphy as an Adjunct for the Diagnosis of Oral Diseases

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Abstract: Bone scintigraphy is a very sensitive method for the detection of osteoblastic activity of the skeleton. The technique consists of imaging the uptake of bone-seeking radiopharmaceuticals, particularly technetium-99m labeled diphosphonates, in the mineral component of bone, which consists of hydroxyapatite crystals and calcium phosphate, as well as in the organic matrix such as collagen fibers. Plain radiographs, computed tomography, and magnetic resonance imaging are classified as structural imaging modalities, whereas bone scintigraphy is a functional method. In many cases, radionuclide imaging techniques are the only means by which early physiologic changes that are a direct result of biochemical alteration may be assessed, before significant bone mineral changes can be detected by other means. Since many oral diseases may cause metabolic changes in the oromaxillofacial complex, it would be of great value to use bone scintigraphy to evaluate more completely some conditions involving the bones in the region to formulate more appropriate treatment plans. Based upon the current literature, the authors discuss the possible applications of bone scintigraphy as a diagnostic and treatment planning adjunct for oral diseases. Bone scintigraphy has proven particularly useful in the study of malignant lesions and in the evaluation of vascularized bone grafts used for maxillofacial reconstructions.

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Key words: bone scintigraphy, oral diseases, radionuclides, dentistry

Submitted for publication 4/23/02; accepted 9/30/02

Conventional and digital radiographs remain the most available tool for the detection of some conditions affecting teeth and bones of the oral cavity. Radiographic examinations display differences in density within an anatomic region and produce images of relatively high resolution. However, in view of the fact that conventional radiologic techniques demonstrate bony changes when there has been an alteration of 30 to 50 percent of the bone mineral content, determination of the extent of some bony lesions by radiologic means alone may become somewhat erroneous.[1] Thus, the x-ray imaging dependence on differential absorption essentially limits this modality to the tissue electron density, which in turn is presented as structural or anatomic changes. Since morphological alterations may simply be later effects of a biochemical process that has remained undetected until the development of physical symptoms, the early diagnosis of a variety of jaw lesions is difficult. Conversely, bone scans have the ability to show reactive modifications in osteoblastic activity that would not appear on radiographic images, but do not show morphologic changes. Although its resolution is not as high as that of radiographs, bone scintigraphy may be positive if there is, approximately, a 10 percent increase in the osteoblastic activity above normal.[2] In many clinical conditions, bone scintigraphy will demonstrate abnormalities long before the radiographs. In other situations, it may demonstrate abnormal changes that may reinforce a questionable radiographic finding. It may also help to determine the metabolic activity within a bone lesion or at its margins.

Scintigraphic images are obtained utilizing the intravenous administration of a radiopharmaceutical, particularly technetium-99m labeled diphosphonates. Technetium-99m have a physical short half-life of six hours, 140keV gamma energy, and the radionuclide-labeled tracers are used in quantities whose emitted radiation doses are far below the amounts that are toxic to human cells.[3] The bone-imaging agents circulate through the bloodstream until they are either incorporated into sites of active bone turnover or are excreted in the urine.[3] The mechanism whereby labeled phosphonates are incorporated into bone is not well understood. Our knowledge of the mechanisms of deposition of the diphosphonates is still incomplete. Phosphate compounds are thought to adsorb to the amorphous bone. In an *in vitro* binding assay, the competitive adsorption of technetium-99m labeled diphosphonates to pure hydroxyapatite is forty times greater than to pure organic bone matrix. Thus, its uptake correlates well with the rate of mineralization.[4]

Image acquisition involves a computed scintillation camera that records the gamma rays emitted by the patient. The camera has a scintillation crystal that fluoresces at the time of interaction with the gamma rays. This fluorescence is detected by photomultiplier tubes, which transform the flashes of light into electronic signals to produce an image that is displayed on a computer monitor.

According to Eggli and Tulchinsky,[5] there are a number of ways to perform a bone scan study. The method chosen is typically influenced by the clinical diagnosis to be evaluated. Bone-imaging techniques include, basically, standard bone scan (whole-body scanning or whole-body spot views), three-phase bone scan, and single photon emission computed tomography (SPECT). Standard bone scans involve the acquisition of static images three hours after tracer administration. Delayed static images may be useful in the evaluation of benign conditions, such as condylar hyperplasia. Three-phase study comprises a flow assessment, a blood pool image, and delayed static views acquisition. The dynamic flow study requires rapid sequential images for sixty seconds during the intravenous administration of the radiotracer. This is followed by a blood pool image reflecting tissue hyperemia and is acquired immediately after the flow study. Three hours after radiotracer administration, the bony uptake of technetium-99m labeled diphosphonates is maximal, and a significant proportion of the unbound tracer will have been excreted by the kidneys. Therefore, the final delayed static images are acquired at this time. Three-phase examinations are frequently performed to evaluate trauma, inflammatory disease, and primary bone tumors. SPECT studies entail acquiring rotating delayed static images, generally sixty-four projections over 360º, followed by computer reconstruction to provide three-dimensional multiplanar slices in the axial, coronal, and sagittal planes, relative to the patient's body. Because of the complex three-dimensional anatomy with extensive overlap of bony structures, the facial bones and base of the skull may be difficult to evaluate with planar bone scan images. In terms of SPECT applications, for instance, temporomandibular joints' internal derangement could be investigated by means of SPECT images.

Bone is an extraordinarily dynamic tissue. Constant turnover in response to metabolic or mechanical demands results in a steady state between new bone formation and resorption. Radionuclide bone scanning takes advantage of this constant physiologic activity. Most morbid processes involving bone result in increased turnover or new bone formation.[6] Scintigraphically, areas of increased bone metabolism are evidenced and appear as areas of increased radiotracer uptake, namely "hot spots." Decreased uptake is associated with metabolically inactive bone, lack of osteogenesis, or an absent vascular supply. With regard to the role of bone turnover in the disease process, scintigraphic findings of decreased uptake indicate lack of reparative response and suggest the presence of a highly aggressive lesion.[7] Zones of photon-deficient or photopenic abnormalities, where there is diminished or absent uptake, are called "cold spots."[6]

Despite the relatively low specificity, previous studies have shown that bone scintigraphy has the potential to provide valuable information concerning the diagnosis and follow-up of several oral conditions such as: primary or metastatic malignancies, benign neoplasms, cystic lesions, inflammatory and infectious processes, metabolic diseases, fibro-osseous dysplasias, hyperplasias, and bone graft viability.[1,7-14]

Primary and Metastatic Malignancies

It is well known that the maxilla and mandible are possible sites for the development of malignant neoplasms, which, on the basis of histological features, are broadly classified into carcinomas and sar-

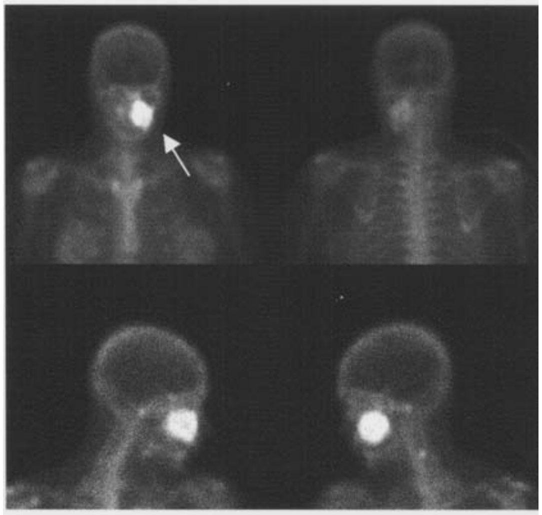

Figure 1. Anterior, posterior, and right and left lateral views, showing an area of intense uptake in the left maxilla that corresponds to an osteosarcoma

comas. Carcinomas found in the jaw may have originated from lesions of the oral mucosa, arise from epithelial residues in the jaw, develop by malignant transformation of a benign lesion, such as a cyst or an ameloblastoma, or be metastatic deposits from primary tumors in distant sites. On the other hand, the great majority of sarcomas are recognized as malignant lesions arising from the mesenchymal tissue components of the jaw.

Oral malignant neoplasms represent approximately 5 percent of all malignant neoplasms in the body.[15] One to 8 percent are considered to be due to metastases.[16] Because of the scarcity of bone marrow in the maxilla and mandible, lesions in the jaw account for less than 1 percent of the overall incidence of bone metastases.[15] Nevertheless, bone metastases to the oral cavity account for approximately 90 percent of all oral metastatic lesions.[15] More than 70 percent of these occur in the mandible, usually in the molar-premolar regions, where the greatest amount of bone marrow is located.[15,16] Adenocarcinomas of the breast, prostate, thyroid gland, lung, kidney, uterus, colon, and stomach are the primary tumors most frequently metastasizing to the maxillofacial region.[15-18]

Söderholm et al.[19] reported that the periosteum has been thought to form a barrier against cancerous invasion of the mandibular bone. However, mandibular bone involvement may occur at an early stage through small defects in the bony cortex of the alveolar process. Since the gingiva is only a few millimeters thick, even a tiny lesion may rapidly spread to the bone.

Considering that malignant tumors in the oral cavity are less common than at other sites in the body and the patient's signs and symptoms may be confused with those related to benign lesions such as odontogenic tumors, the early diagnosis of carcinomas and sarcomas of the jaw often poses clinical challenges. Indeed, the definitive method to diagnose malignant neoplasms is histopathologic examination. However, the superior sensitivity of bone scintigraphy in providing valuable information for preoperative assessment of the malignant lesions' extent has been reported by many authors.[11,13,15-20]

The most frequently encountered scintigraphic pattern in malignant bone lesions is that of one or multiple randomly distributed foci of intensely in-

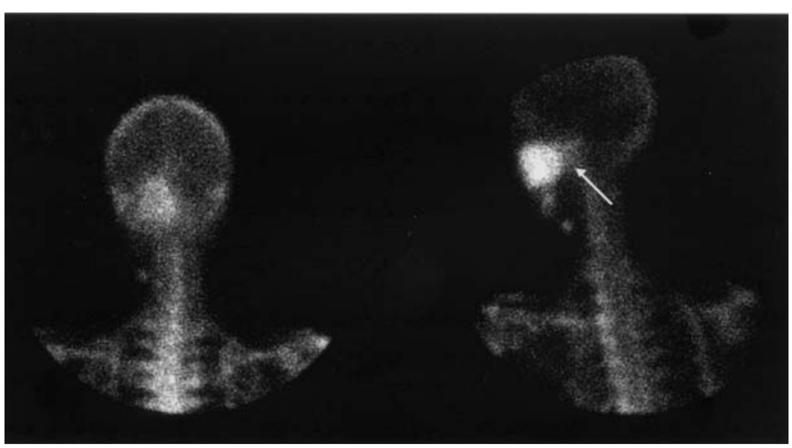

Figure 2. The oblique view suggests that the osteosarcoma, illustrated in Figure 1, has extended to the maxillary tuberosity

creased radiotracer uptake, the so-called "hot spots" (Figures 1 and 2).

Inflammatory and Infectious Processes

Inflammation represents a dynamic process that takes place in the connective tissue as a reaction to intrinsic and/or extrinsic agents. Accordingly, some oral conditions such as osteomyelitis, traumatic injuries, osteoarthritis, periapical lesions, and periodontal disease play an important role in bone metabolism and result in a positive bone scan image. Figure 3 illustrates the features of an acute osteomyelitis, as demonstrated by an intense technetium-99m labeled diphosphonate uptake in the right posterior maxillary region, that developed following a tooth extraction.

Diagnostic approaches of pulpo-periapical diseases usually are based on the patient's symptoms and mainly on clinical and radiographic findings, rather than on bone scan imaging. Nevertheless, bone scintigraphy may disclose periapical lesions because the radionuclide uptake may precede radiographic alterations by months. Baumgartner and Eggli[10] reported the detection of a periapical lesion of endodontic origin in the mandible during a routine bone scan used as a follow-up to cancer therapy. Matteson et al.[8] explained that some undiscovered dental diseases may be identified if the nuclear physicians are aware of this possibility and request appropriate dental examination for the affected patients.

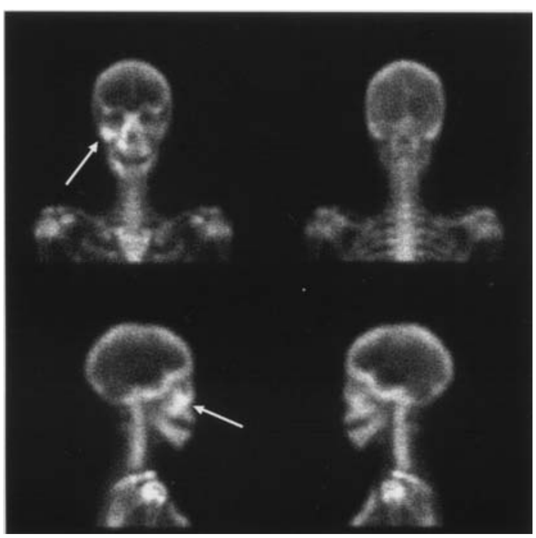

Figure 3. Anterior, posterior, and right and left lateral images, showing increased uptake of technetium-99m labeled diphosphonate, which reflects the activity of an infectious process

The usefulness of the bone scan as a diagnostic aid for inflammatory responses of the temporomandibular joints (TMJ) is somewhat controversial.[2,11,21] However, attempts have been made to improve the evaluation of the metabolic and physiological status of TMJ bony structures. In fact, bone scans may demonstrate inflammatory reactions that take place in TMJ bony structures, as illustrated in Figure 4. Pogrel et al.[22] designed a prospective study to compare single-photon emission computed tomography (SPECT) imaging with lateral planar images for quantitative assessment of pathologic processes of the mandibular condyle. These authors not only highlighted the efficiency of the SPECT technique, but also suggested that it could replace planar images. SPECT bone scanning offers both enhanced image contrast resolution and more accurate localization of active disease as it provides three-dimensional information, allowing the interpreters to visualize in transaxial, coronal, and sagittal slices, structures that would overlap on planar views.

Bouquot and LaMarche[23] undertook a retrospective investigation of some processes that they diagnosed as ischemic osteonecrosis in patients with histories of endodontic treatment, tooth extraction, or fixed partial denture pontics in areas of idiopathic pain. According to these authors, ischemic osteonecrosis, which is the result of a wide variety of local and systemic disorders that eventually lead to ischemia and infarction of the cancellous bone, is often undiagnosed due to the high proportion of false-negative radiographic images. On the other hand, bone scans may reveal occult abnormalities as "hot spot" areas in the subpontic bone.[23]

Fibro-Osseous Dysplasias

Fibrous dysplasias of the jaw are believed to be benign, self-limiting, but non-encapsulated, lesions occurring mainly in young subjects. Histologically, they are characterized by the replacement of normal bone by a cellular fibro-osseous tissue containing islands or trabeculae of metaplastic bone. Although jawbone fibrous dysplasias are usually monostotic lesions, they may occasionally be part of a polyostotic process.[24] Enlargement of the lesions is slow and insidious and persists until cessation of

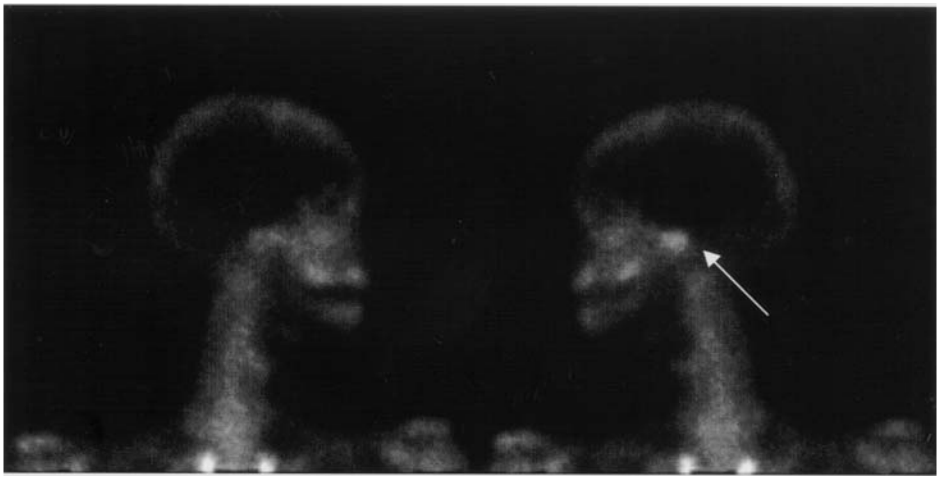

Figure 4. Right and left lateral views showing an area of intense uptake in the left TMJ, in a patient with degenerative joint disease

growth, even though in some cases it may continue into adulthood. The treatment of choice is conservative osseous contouring by surgery, and its goal for larger lesions should be correction of esthetic and functional problems.[24]

Radiographs are usually adequate for the diagnosis; however, bone scintigraphy is often useful to establish the extent and activity of maxillofacial lesions.[11] Figure 5 shows a planar image of an adult patient for whom surgical treatment was considered. It was not possible to determine if growth of the lesion had ceased, and thus the patient was referred for a nuclear medicine bone scan. The focal "hot spot" in the right mandibular body demonstrated that the lesion was still metabolically active.

Bone Graft Viability

Osseointegrated implants are now accepted as a modality of treatment to replace missing teeth for an ever-increasing segment of the population. The success of this kind of rehabilitation relies on the quality and amount of remaining osseous tissue. It is sometimes necessary to apply bone grafts to ensure adequate bone support for the implants. Bone grafts are also employed to replace parts of the jaw compromised by problems such as periodontal disease, trauma, tumor infiltration, cystic lesions, serious infections, or congenital defects.

Harbert[11] mentioned that bone scintigraphy provides a means of predicting graft failure before radiographic or clinical changes become apparent and, thus, helping to avoid a loss of surrounding bone from graft necrosis or infection. It is especially useful in reconstruction of the jaw that usually involves a vascularized bone autograft, because clinical monitoring of the transplanted bone is difficult. Kärcher et al.[9] reported their experience with the use of three-phase bone scintigraphy in assessing the post-operative viability of seven vascularized bone grafts. According to these authors, in all successful cases, a positive bone scan correlated with a viable bone graft. Two negative exams, show-

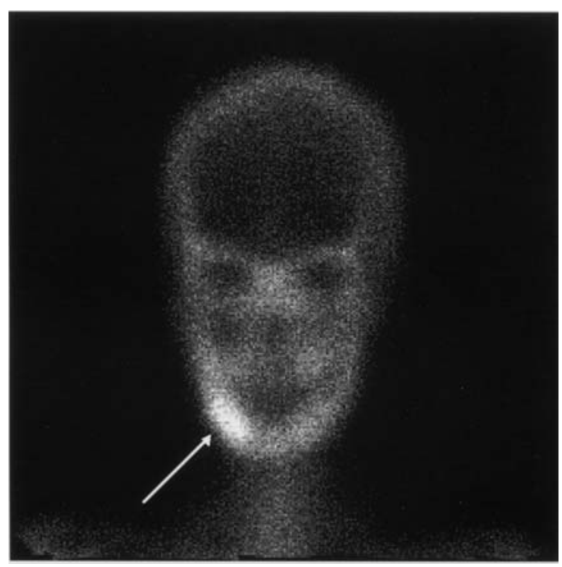

Figure 5. Anterior view showing a focal area of increased uptake localized to the right mandible body, which demonstrates that the fibrous dysplasia still has an active growth pattern

ing photopenic defects, corresponded to nonviable grafts that had to be removed.

Recently, Schimming et al.[14] discussed the use of computer-aided three-dimensional reconstruction of SPECT images in the assessment of vascularized bone grafts, in the early post-operative period and approximately two weeks after surgery. The authors stated that modern-day SPECT scanning of the head and neck area, including computer-aided three-dimensional SPECT reconstruction, is useful to evaluate microvascular success or failure and that computer-aided three-dimensional SPECT reconstruction adds significantly to the value of planar bone scintigraphy and conventional SPECT images, particularly because it allows a better description of the bone graft, since it provides images with even higher contrast, without any superimposing effects.[14] However, because of bone remodeling immediately after surgery, it is not a completely reliable method for the early assessment of microvascular patency in vascularized bone grafts.

Discussion

Although a variety of health care professionals may provide a multitude of diagnostic and therapeutic services, the dentist undertakes the responsibility of ordering the appropriate treatment for the oral diseases or referring the patient to another specialist. Therefore, dentists should have a basic knowledge of the principles of diagnostic imaging modalities and possible clinical applications.

Routinely, after a comprehensive case history and clinical examination, dentists prescribe radiography. To investigate diseases related to the teeth and maxillofacial bones, radiographs are currently more available and less expensive than bone scintigraphy and patients are more willing to undergo radiography than scintigraphy. On the other hand, bone scintigraphy is of proven value as an additional diagnostic tool in radiographic examinations of skeletal disorders. Each imaging modality provides its own specific information. Imaging studies such as radiography, computed tomography (CT), magnetic resonance imaging (MRI), and ultrasound (US) serve to display both normal and morbid anatomy and physiology.[6] This is important because a fundamental part of classic clinical evaluation and many forms of treatment also rely on anatomic localization and characterization of diseases. From a multimodality imaging perspective, detection of skeletal physiology is the greatest strength of bone scintigraphy.

Bone scintigraphy is a physiologic method, which is more sensitive than radiography. In terms of diagnostic approach, the major disadvantage of bone scintigraphy, in relation to radiography, is its nonspecificity. It is reasonable to assume, therefore, that an integrated approach of correlating the results of both procedures might reduce the individual limitations of each.

Carrera and Collier Jr.[6] explained that all diagnostic tests, including imaging modalities, serve three fundamental purposes in evaluating bone diseases: detection, characterization, and staging. Structural imaging modalities such as radiography, CT, and MRI should be used in conjunction with bone scintigraphy, which shows modifications in the osteoblastic activity. A good example is the diagnosis of condylar hyperplasia, on the basis of radiographic examination, in patients having facial asymmetry with deviation of the mandible. One goal of TMJ scintigraphy is to, in fact, determine whether bone growth has ceased prior to treatment. Patients with equal uptake on the right and the left sides show no further progression of the asymmetry and may undergo treatment.[25]

Scintigraphic bone studies may be important in determining the extent of some benign lesions such as odontogenic keratocyst, ameloblastoma, and odontogenic myxoma.[1,7] With respect to the malignant neoplasms, these entities usually display an elevated radionuclide uptake, and the disease process may extend considerably beyond the zone of visible bone destruction shown on the radiographs. Thus, bone scintigraphy may be useful in justifying larger resections in order to achieve complete excision and avoid recurrence.[7] According to Meidan et al.,[26] bone scanning is also a valuable test in the follow-up of peri-implant bone tissue. But a relatively less expensive and invasive method, digital subtraction radiography (DSR), has also proven reliable in assessing dental implants osseointegration.[27] Specifically in this case, in our opinion, bone scan should not be indicated.

In conclusion, dentists should be aware that, similar to other imaging methods, bone scintigraphy has its advantages and disadvantages and may sometimes fail in completely solving a diagnostic problem. For a proper diagnostic approach and follow-up, morphologic and physiologic imaging modalities, in combination, should support each other in offering valuable information in the diagnosis of maxillofacial jaw bone lesions.

REFERENCES

1. Lurie AG, Puri S, James RB, et al. Radionuclide bone imaging in the surgical treatment planning of odontogenic keratocysts. Oral Surg Oral Med Oral Pathol 1976;42:726-30.
2. Craemer TD, Ficara AJ. The value of the nuclear medical scan in the diagnosis of temporomandibular joint disease. Oral Surg Oral Med Oral Pathol 1984;58:382-5.
3. Subramanian G. Radiopharmaceuticals for bone scanning. In: Collier Jr BD, Fogelman I, Rosenthall L, eds. Skeletal nuclear medicine. St. Louis: Mosby, 1996:9-20.
4. Francis MD, Horn PA, Tofe AJ. Controversial mechanism of technetium-99m deposition on bone. J Nucl Med 1981;22:72.
5. Eggli DF, Tulchinsky M. Normal planar bone scan. In: Collier Jr BD, Fogelman I, Rosenthall L, eds. Skeletal nuclear medicine. St. Louis: Mosby, 1996:23-44.
6. Carrera GF, Collier Jr BD. A multi-modality approach to bone imaging. In: Collier Jr BD, Fogelman I, Rosenthall L, eds. Skeletal nuclear medicine. St. Louis: Mosby, 1996:73-84.
7. Josell SD, Reiskin AB, Gross BD. Dentigerous cyst with mural ameloblastoma. J Am Dent Assoc 1979;99:634-6.
8. Matteson SR, Staab EV, Fine JT. Bone-scan appearance of benign oral pathologic conditions. J Oral Surg 1980;38:759-63.
9. Kärcher H, Füger G, Borbely L. Bone scintigraphy of vascularized bone transfer in maxillofacial surgery. Oral Surg Oral Med Oral Pathol 1988;65:519-22.
10. Baumgartner JC, Eggli D. The use of bone imaging to detect a periapical lesion of endodontic origin. J Endod 1989;15:493-5.
11. Harbert JC. The musculoeskeletal system. In: Harbert JC, Eckelman WC, Newmann RD, eds. Nuclear medicine: diagnosis and therapy. New York: Thieme, 1996:801-63.
12. Frederiksen NL. Specialized radiographic techniques. In: White SC, Pharoah MJ, eds. Oral radiology: principles and interpretation. St. Louis: Mosby, 1999:217-40.
13. Schimming R, Juengling FD, Lauer G, et al. Computer-aided 3-D ^{99m}Tc-DPD-SPECT reconstruction to assess mandibular invasion by intraoral squamous cell carcinoma: diagnostic improvement or not? J Craniomaxillofac Surg 2000;28:325-30.
14. Schimming R, Juengling FD, Lauer G, et al. Evaluation of microvascular bone graft reconstruction of the head and neck with 3-D ^{99m}Tc-DPD SPECT scans. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2000;90:679-85.
15. Stavropoulos MF, Ord RA. Lobular adenocarcinoma of breast metastatic to the mandibular condyle. Oral Surg Oral Med Oral Pathol 1993;75:575-8.
16. Aniceto GS, Peñín AG, Pages RM, et al. Tumors metastatic to the mandible: analysis of nine cases and review of the literature. J Oral Maxillofac Surg 1990;48:246-51.
17. Carmichael FA, Mitchell DA, Dyson DP. Case report: two contrasting radiological presentations of prostatic adenocarcinoma in the jaws. Dentomaxillofac Radiol 1996;25:283-6.
18. Glaser C, Lang S, Pruckmayer M, et al. Clinical manifestations and diagnostic approach to metastatic cancer of the mandible. Int J Oral Maxillofac Surg 1997;26:365-8.
19. Söderholm AL, Lindqvist C, Hietanen J, et al. Bone scanning for evaluating mandibular bone extension of oral squamous cell carcinoma. J Oral Maxillofac Surg 1990;48:252-7.
20. Ventä I, Oikarinen VJ, Söderholm AL, et al. Third molars confusing the diagnosis of carcinoma. Oral Surg Oral Med Oral Pathol 1993;75:551-5.
21. Harris SA, Rood JP, Testa HJ. Post-traumatic changes of the temporo-mandibular joint by bone scintigraphy. Int J Oral Maxillofac Surg 1988;17:173-6.
22. Pogrel MA, Kopf J, Dodson TB, et al. A comparison of single-photon emission computed tomography and planar imaging for quantitative skeletal scintigraphy of the mandibular condyle. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1995;80:226-31.
23. Bouquot JE, LaMarche MG. Ischemic osteonecrosis under fixed partial denture pontics: radiographic and microscopic features in 38 patients with chronic pain. J Prosthet Dent 1999;81:148-58.
24. Langlais RP, Langland OE, Nortjé CJ, eds. Diagnostic imaging of the jaws. Philadelphia: Williams & Wilkins, 1995:565-615.
25. Cisneros GJ, Kaban LB. Computerized skeletal scintigraphy for assessment of mandibular asymmetry. J Oral Maxillofac Surg 1984;42:513-20.
26. Meidan Z, Weisman S, Baron J, et al. Technetium 99m-MDP scintigraphy of patients undergoing implant prosthetic procedures: a follow-up study. J Periodontol 1994;65:330-5.
27. Brägger U. Use of radiographs in evaluating success, stability and failure in implant dentistry. Periodontol 2000 1998;17:77-88.