WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL SCIENCES

SJIF Impact Factor 7.421

Volume 7, Issue 11, 558-569 Review Article ISSN 2278 – 4357

FUSION IMAGING IN HEAD AND NECK - DENTISTS' PERSPECTIVE

Dr. Saraswathi Gopal K. MDS*[1] and Dr. A. Vani Anusha[2]

[1]Professor and Head of the Department, Department of Oral Medicine and Radiology, Meenakshi Ammal Dental College, Chennai, 95.

[2]Post Graduate Student, Department of Oral Medicine and Radiology, Meenakshi Ammal Dental College, Chennai, 95.

Article Received on
17 September 2018,

Revised on 07 October 2018,
Accepted on 28 Oct. 2018,

DOI: 10.20959/wjpps201818-12603

***Corresponding Author**
Dr. Saraswathi Gopal K. MDS
Professor and Head of the Department, Department of Oral Medicine and Radiology, Meenakshi Ammal Dental College, Chennai, 95.,

ABSTRACT

Molecular imaging is an essential component of the clinical decision-making tree. With the advent of newer and multimodality imaging techniques, the existent medical imaging technologies represent the leading component of health care institution and have a pivotal role in the daily clinical management of patients. Both functional and anatomical information are essential in state-of-the-art patient management. An appreciation for this type of combined information is best illustrated with the introduction of the term "anato-metabolic imaging". Film radiography, diagnostic ultrasonography, Computed Tomog-raphy (CT) and Magnetic Resonance Imaging (MRI) are commonly used morphologic imaging techniques, which mainly require a macroscopic anatomic change for information to be recorded by an image receptor. However, in some human diseases abnormal biochemical processes either occur without any evident anatomic change or occur prior to it. Nuclear imaging provides an avenue to the radiologist to assess such physiologic/biochemical changes and also assists in differentiating between metabolically dying or deceased cells and those which are actively metabolizing. The realization that the information provided by anatomic (CT and MR) and molecular/ nuclear imaging modalities is complementary spurred the development of various strategies for multimodality image registration and fusion. Correlative or fusion functional-anatomic imaging is now well established and its clinical value widely recognized in various fields of medicine and in particular the discipline of oncology. The current article aims at delivering a keynote on available hybrid imaging techniques and their contemporary applications in various disciplines of medicine and oromaxillofacial imaging.

KEYWORDS: Hybrid Imaging, Fusion Imaging, Positron Emission Tomography (PET), Single Photon Emission Tomography (SPECT), Head And Neck Oncology, Non Neoplastic Fusion Imaging.

INTRODUCTION

Evolution of medical imaging was rapid during the last few decades and the practice of medicine has become an inexorable consequence to this growth.[1] Film radiography, diagnostic ultrasonography, Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) are commonly used morphologic imaging techniques, which mainly require a macroscopic anatomic change for information to be recorded by an image receptor. However, in some human diseases abnormal biochemical processes either occur without any evident anatomic change or occur prior to it. Nuclear imaging provides an avenue to the radiologist to assess such physiologic/biochemical changes and also assists in differentiating between metabolically dying or deceased cells and those which are actively metabolizing.[2]

Nuclear medicine is the medical speciality using small amounts of radioisotopes or radiopharmaceuticals as tracers to diagnose the disease. These tracers when injected into the body, shows affinity to the metabolically altered sites and they further emit characteristic radiations, which will be captured by special electronic instruments like scintillation or gamma camera.[2,3] Commonly used nuclear medical imaging modalities are Scintigraphy, SPECT (Single photon emission computed tomography) and PET (Positron emission tomography). Several radioactive tracers can be used to image metabolically active tissues in physiologic imaging. Currently, the most commonly used tracer with PET is 18-fluorodeoxyglucose (FDG). FDG is a radioactively labelled glucose analog that is taken up by tissue in the same fashion as normal glucose, thus becoming concentrated in cells with high glucose utilization. Single-photon emission computed tomography (SPECT), the predecessor of PET, uses FDG or technetium-99m methoxyisobutylisonitrile (Tc-MIBI) as tracers. Tc-MIBI is a cationic and lipophilic molecule that accumulates in tissues with high mitochondrial content, including neoplastic cells and myocardium.

Molecular imaging using high-resolution single-photon emission computed tomography (SPECT), and positron emission tomography (PET) has advanced elegantly and steadily gained importance and eventually has held an assurance in the diagnostic, clinical and research arenas.[2,4] These modalities can also reconstruct three dimensional (3D) images of the structures and thus have improvised the diagnostic efficacy, especially in the field of oncology.

Disease originates from physical distress as well as from changes in the molecular and physiological level. In most cases of serious diseases, early diagnosis is key and therefore, imaging the anatomy of a patient may not suffice in making a correct and timely diagnosis. Therefore, a combination of imaging techniques during the course of diagnosis and subsequent treatment to monitor the patients is a requisite. In other words, both functional and anatomical information are essential in state-of-the-art patient management.[5,6] The advantages of integrated, anato-metabolic imaging are manifold.[7]

This descriptive review emphasizes the tenor on current literature of hybrid imaging, the chief intent of fusion in the epoch of imaging and its applications pertaining to head and neck in general and orofacial panaroma in particular.

Objective and Biophysics behind fusion

Hybrid imaging bestows PET images that are often fused with contrast-enhanced computed tomography (CT) images to facilitate anatomic localization of the radiopharmaceutical.

Diagnostic contrast enhanced CT scan (CECT) has become an essential part of PET-CT scans that provide images with both the anatomical as well as functional aspects of the disease process. Historically, medical devices to image either anatomical structure or functional processes have developed along somewhat independent paths. The recognition that combining images from different techniques can nevertheless offer significant diagnostic advantages gave rise to sophisticated software techniques to co-register structure and function retrospectively.[8,9] The usefulness of combining anatomical and functional planar images was evident to physicians as early as the 1960s.[10] In addition to simple visual alignment, or the use of stereotactic frames that are undesirable or inconvenient for diagnostic imaging, sophisticated image fusion software was developed from the late 1980s onwards. Alternatives to software-based fusion have now become available through instrumentation that combines two complementary imaging techniques within a single gantry, an approach that has since been termed "hardware fusion". A combined, or hybrid, tomograph such as SPECT/CT or PET/CT can acquire co-registered structural and functional information within a single study.

The data are complementary allowing CT to accurately localize functional abnormalities and SPECT or PET to highlight areas of abnormal metabolism.[5] MRI with its exquisite soft tissue resolution is the ideal choice for morphological imaging of many tumors, particularly in the central nervous system (CNS) and musculoskeletal system. Routinely performed technique is to achieve PET and MRI scans and fusing the MR images with PET images using various softwares. This technique has limitations including changes in patient's position and different scanning parameters (like FOV, slice thickness) with separate MRI and PET scanning, resulting in delusive fusion images.[11]

Applications of Fusion Imaging

Applications of fusion imaging had become pervasive and can be broadly categorized into oncological and non-oncological applications.

Hybrid Imaging in Oncology

- It is helpful in not only detecting the osseous metastases but also involvement of other visceral organs which renders the technique of fusion imaging superior to MDP (methylene di phosphste) bone scan.[12]
- F18-FDG radiopharmaceutical is used to assess the metabolic activity of malignant lesions and also for the evaluation of treatment response of the tumor.[13]
- F18-choline is used to identify any lesion with high choline (which is a cell membrane proliferation marker) content, similar to MR spectroscopy which has several technical limitations.[14]
- F18-angiography can be used for assessing the neovascularisation of the tumors, similar to CT and MR perfusion. CT and MR perfusion scans are technically limited as whole body scan is not possible.[15]
- PET-MRI has applications mainly in head and neck imaging especially in CNS tumors.[16]

Fusion imaging in head and neck carcinomas

Early diagnosis and accurate staging of head and neck squamous cell carcinoma (HNSCC) can strongly influence the prognosis. The use of traditional tomographic imaging modalities, CT and magnetic resonance imaging (MRI) has greatly improved staging and monitoring for HNSCC. However, small metastases and early recurrent disease can still be overlooked.[17] Hybrid PET/CT imaging allows fusing of the anatomic data of CT with the functional information of PET, offering improved localization of metabolic abnormalities and thus, more accurate detection of malignant lesions in the head and neck.[18,19,20] Further, the false-positive (FP) values associated with PET imaging can be significantly reduced in favor of the positive predictive values (PPV) by the integration of CT. Moreover, the CT component of fusion imaging is used for the attenuation correction of the PET data, which shortens the overall acquisition time by almost 20 min. Sensitivity and specificity rates for the detection of nodal metastasis in HNSCC were 100% and 87.5% for PET/CT, respectively. In the post-therapy setting, the PET/CT technology is helpful in differentiating a recurrent or residual tumor from post-therapy inflammatory changes.[21] There has been a growing interest in the use of PET/ CT-guided intensity-modulated radiotherapy (PET/CTguided IMRT) for tumor contouring, allowing for accurate delineation of the target volume and sparing of normal tissues for effective radiation therapy, because of its ability to provide both anatomic and functional information.

Clinical examination and tomographic imaging modalities are often insufficient to detect early or subtle changes in a treated neck, as postsurgical and postradiation inflammatory changes can complicate the identification of recurrent or residual disease. PET/CT can detect and differentiate radiation and surgical changes from residual or recurrent tumors because cancer cells retain more FDG for longer periods of time than inflammatory tissues. Recent studies have shown that PET/CT had a sensitivity of more than 90% for localization of recurrent disease.[22] Patients with primary HNSCC (head and neck squamous cell carcinoma) are at a high risk of developing additional primary cancers in the aerodigestive tract as a result of field cancerization phenomena. Second primary lesions occur either around the same time as the first primary tumor (synchronous tumor) or after a short interval (metachronous tumor). Panendoscopy at regular intervals following treatment has not been shown to be effective in detecting second primaries; as a result, treatment guidelines tabulated by the American Head and Neck Society do not recommend routine post-treatment panendoscopy. PET/CT has proven useful in the detection of second primary tumors in patients previously treated for HNSCC and being watched for recurrence. However, some debate still exists on the optimal timing of the first surveillance scan. Early scanning with PET/CT has low sensitivity and specificity because there may be residual viable tumor cells that are stunned from radiotherapy; moreover, FDG uptake in the early posttreatment period may reflect post-operative or post-radiotherapy inflammation. Therefore, a considerable amount of recent data suggests that initial PET/CT surveillance as early as 8 weeks after completion of therapy may yield highly sensitive and specific information regarding the presence of residual neoplasm, distant metastases, or a second primary tumor (sensitivity, 90.9%; specificity, 93.3%).[23]

The use of SPECT/CT device is particularly advantageous in nuclear oncology where SPECT scan is aimed at detecting mostly soft tissue lesions and the localization and identification of organ involvement is extremely difficult without morphological investigation. However, it can be made much more precise with co-evaluation of SPECT and CT image sections.[24,25] Bone scintigraphy with adjunct SPECT/CT significantly improves the specificity, the exact classification of lesion etiology.[26,27] Another significance of SPECT/CT device is the possibility of applying absorption and motion-correction. Because gamma-rays from patients passing through the tissues are partially absorbed depending on the thickness images resulting in false positivity may be obtained. The application of absorption correction of X-ray through elimination of artifacts, the three-dimensional (3D) and four-dimensional (4D) image display or the possibility of 3D printing in the near future significantly increases and will increase the specificity of diagnostics and also the effectiveness of the therapy.[28,29]

NON-ONCOLOGICAL APPLICATIONS

Infection and Inflammation

F18-FDG PET-CT utilizes the fact that activated mononuclear cells and neutrophilic granulocytes are associated with infection-respiratory burst [large quantities of glucose being utilised through hexose monophosphate shunts] resulting in higher FDG uptake in infection. Besides this, physiologic FDG uptake in the hematopoietic marrow is relatively low thus making PET-CT a promising imaging technique in acute as well as chronic non-osseous and osseous inflammatory and infectious diseases of the extremities as well as of the trunk.[30,31] PET-CT is of great advantage in patients with pyrexia of unknown origin (PUO) and occult malignancy.[32,33]

Osteomyelitis is a bone infection and is usually caused by bacterial, fungal, or mycobacterial microorganisms. Osteomyelitis can be subdivided into the acute, subacute, or chronic type based on the time course of disease. Acute osteomyelitis usually does not pose a diagnostic challenge to clinicians, as systemic symptoms such as fever, fatigue, and malaise along with localized signs including reduced motion, pain, and tenderness of the involved bone usually aid in making the correct diagnosis. However, the accurate diagnosis of subacute or chronic osteomyelitis is often difficult by physical examination and existing radiological or nuclear medicine techniques, particularly when there are preexisting alterations in osseous structures due to previous trauma or surgery. Although the use of radiolabeled WBC imaging in combination with bone marrow scintigraphy has been reported to be highly accurate for detecting chronic osteomyelitis, the role of these scintigraphic techniques appears to be limited in most clinical settings.[34] Osteomyelitis of the jaw can be a difficult disease to treat because the chronic forms have a marked tendency towards recurrence. Positron Emission Tomography (PET) scans using flurodeoxy glucose F18 have shown promising results in the diagnosis of osteomyelitis of the jaws, especially when combined with traditional CT scans. These 2 modalities fuse the anatomic structures and a metabolic state, thereby obtaining a 3D image with high sensitivity and specificity. Individual PET scans have a much higher rate of false-negative and false-positive results. As this is a relatively novel diagnostic approach, additional research is needed.[35]

In the soft tissue infections, discrimination of active infectious lesions from residual changes due to cured processes or postoperative changes can be early detected by PET-CT. Functional changes caused by activation of inflammatory cells does not depend on morphologic changes, hence it helps in monitoring treatment response. It also helps in identifying multiple lesions and selection of the appropriate biopsy site.[36]

Neurological applications

Apart from neuro-oncology, fusion imaging has applications in epilepsy and dementia imaging.[37] Among the neurological diseases, CT and MR studies detect unsuspected clinically significant lesions in only 5% of patients with dementia. However, PET/CT has been found useful in evaluating patients with multi-infarct dementia, Parkinson's disease and Ictal phase imaging. A metabolically active mass in the brain or spinal cord can be well delineated morphologically by MRI. Hypometabolic areas of brain can be the epileptogenic foci in interictal phase F18-FDG PET imaging. These foci can be better localized on high resolution MR images fused with PET scans. Also, MR-tractography images can be fused with PET images as well as routine MR images to demonstrate foci of white matter and grey matter hypertrophy corresponding to hypometabolic area on PET. Ictal phase PET imaging demonstrates these foci to be hypermetabolic. F18-FDG PET demonstrates changes of Alzheimer's disease as focal hypometabolic areas in the temporal lobes. These images can be fused with MR images to visualize the actual areas involved.[37,38]

Fusion imaging in Temporomandibular Joint Disorders (TMDS)

Orofacial pain resulting from temporomandibular disorders has a negative impact on the quality of life of patients. Temporomandibular joint dysfunctions (TMD) are defined as a group of multifactorial disorders that involve a variety of clinical alterations and chronic pain in the masticatory muscles, temporomandibular joints (TMJ), and adjacent structures.

Radiography, computed tomography (CT) and magnetic resonance imaging (MRI) are helpful in the evaluation of anatomy of the region and aid diagnosis. However, observation of local metabolic alterations is accurately enabled with nuclear imaging techniques.

Bone scintigraphy evaluates the rate of metabolic activity of the skeleton through the use of radiopharmaceuticals, whose concentration in the bone depends on the local blood flow, vascular permeability, enzymatic action, amount of mineral component of the bone, and of immature collagen. This concentration is proportional to the rate of bone remodelling.

A study by Coutinho et al. (2006) aimed at assessing the contribution of fused SPECT/CT images using 99mTc-MDP to diagnose patients with suspected TMD. Their results showed that 99mTc-MDP SPECT/CT in the TMJ region is a relevant complementary investigation which is useful, sensitive, specific and an accurate radio-nuclear examination and that it may be one of the methods of choice for TMD diagnosis. Thus, the applications of this method must be further investigated and compared with other imaging diagnostic methods. Also, the applications of 99mTc-MDP SPECT/CT to the evaluation of therapy results and follow-up of TMD patients must be further investigated.[39]

Fusion imaging in salivary gland pathology

Radionuclide imaging is a rarely used technique for salivary gland imaging. Sodium pertechnetate (Tc $^{(99)}$) is actively concentrated and secreted by salivary gland cells while it is not taken up by majority of neoplastic lesions, hence the latter appear as *cold spots*. Warthin's tumor is an exception to the rule and appears as a *hot spot.* Actively dividing cells take up Gallium-67; hence it is useful in detecting diffuse inflammatory/neoplastic processes such as sarcoidosis and lymphoma. Positron emission tomography (PET) imaging using 2-deoxy-2-[18F] fluoro-deoxy-glucose (FDG) can be used to differentiate benign from malignant tumors of the salivary glands as the former appear as *cold spots* with the exception of Warthin's tumor and oncocytoma.[40,41]

A study by Verena Ruhlmann (2017), evaluated the value of 18F–FDG PET/CT (PET/CT) and MRI for local and/or whole-body restaging of adenoid cystic carcinoma of the head and neck (ACC). Their results depicted that the sensitivity of PET/CT and MRI was 96% (89%), specificity 89% (89%) and accuracy 94% (89%) for detection of local tumors. Additionally, PET/CT revealed lymph node metastases in one patient and distant metastases in 9 out of 36 patients. In three patients secondary primaries were found. They concluded that whole-body PET/CT in addition to MRI of the head and neck improves detection of local tumour and metastastic spread in ACC.[42]

CONCLUSION

Imaging fusion is the process that allows the integration of the functional information of nuclear medicine studies with the anatomic strengths of structural modalities, providing the solution to a variety of clinical problems in diagnosis, treatment planning. SPECT/CT and PET/CT are recently developed dual-modality, combined functional/ morphologic imaging devices. They are able to overcome some drawbacks of conventional image fusion approaches and are routinely utilizable. The data available in oncological applications clearly indicate that these technologies improve scintigraphic imaging interpretation and affect clinical strategies. Their role in head and neck oncology has become pivotal. In addition, other applications in evaluating infections, inflammatory and non inflammatory clinical enigmas of head and neck employs fusion imaging which harbors radio-nuclear imaging an advanced multimodality imaging of choice.

REFERENCES

1. Zaidi H, Montandon ML, Alavi A. The clinical role of fusion imaging using PET, CT, and MR imaging. PET clinics, 2008 Jul 1; 3(3): 275-91.
2. Sahithi D, Reddy S, JyothirmaiKoneru M, Satheesh G. Nuclear Imaging in Dentistry-A novel modality to explore.
3. Boloor V, Hosadurga R, Pratap S, Rao A. Nuclear medicine in dentistry revisited: New avenues to explore. Clinical Cancer Investigation Journal, 2013 Jul 1; 2(3): 189.
4. Mushtaq S. Role of nuclear medicine in dentistry. Glob J Med Public Health, 2012; 1: 1-4.
5. Beyer T, Freudenberg LS, Townsend DW, Czernin J. The future of hybrid imaging—part 1: hybrid imaging technologies and SPECT/CT. Insights into imaging, 2011 Apr 1; 2(2): 161-9.
6. Wahl RL et al “Anatometabolic” tumor imaging: fusion of FDG PET with CT or MRI to localize foci of increased activity. J Nucl Med, 1993; 34: 1190–1197.

7. Townsend D Multimodality imaging of structure and function. Phys Med Biol, 2008; 53(4): R1–R39.
8. Hutton BF, Braun M Software for image registration: algorithms, accuracy, efficacy. Semin Nucl Med, 2003; XXXIII(3): 180- 192.
9. Slomka P, Baum R Multimodality image registrationn with software: state-of-the-art. Eur J Nucl Med Mol Imaging, 2009; 36(Suppl 1): S44–S55.
10. Wagner HN A personal history of nuclear medicine. Springer, London, 2005.
11. Mallarajapatna GJ, Rastogi R. Fusion Imaging: The Current Trends. JIMSA, 2013; 26(1): 73-5.
12. Ozulker T, Uzun, AK, Ozulker F, Ozpacac T. Comparison of 18F-FDG-PET/CT with 99mTc-MDP bone scintigraphy for the detection of bone metastases in cancer patients. Nuclear Medicine Communications, 2010; 31(6): 597-603.
13. Britz-Cunningham SH, Millstine JW, Gerbaudo VH. Improved discrimination of benign and malignant lesions on FDG PET/CT, using comparative activity ratios to brain, basal ganglia, or cerebellum. Clin Nucl Med, 2008; 33 (10): 681-7.
14. Beheshti M, Vali R, Waldenberger P, Fitz F, Nader M, Hameer J, et al. The use of F-18 choline PET in the assessment of bone metastases in prostate cancer: correlation with morphological changes on CT. Mol Imaging Biol 2010; 12 (1): 98-107.
15. Ledezma CJ, et al. 18F-FDOPAPET/MRI fusion in patients with primary/recurrent gliomas: Initial experience, Eur J Radiol, 2008; doi:10.1016/j.ejrad.2008.04.018.
16. Jacobs AH, Kracht LW, Gossmann A, Ruger MA, Thomas AV, Thiel A, et al. Imaging in Neurooncology. Neuro Rx, 2005; 2(2): 333-347.
17. Forastiere A, Koch W, Trotti A, Sidransky D. Head and neck cancer. N Engl J Med, 2001; 345: 1890-900.
18. Antoch G, Vogt FM, Freudenberg LS, Nazaradeh F, Goehde SC, Barkhausen J, et al. Whole-body dual-modality PET/CT and whole-body MRI for tumor staging in oncology. JAMA, 2003; 290: 3199-206.
19. Ha PK, Hdeib A, Goldenberg D, Jacene H, Patel P, Koch W, et al. The role of positron emission tomography and computed tomography fusion in the management of early-stage and advanced-stage primary head and neck squamous cell carcinoma.Arch Otolaryngol Head Neck Surg., 2006; 132: 12-6.
20. Suzuki H, Hasegawa Y, Terada A, Ogawa T, Hyodo I, Suzuki M, et al. Limitations of FDG-PET and FDG-PET with computed tomography for detecting synchronous cancer in pharyngeal cancer. Arch Otolaryngol Head Neck Surg., 2008; 134: 1191-5.

21. Branstetter BF 4th, Blodgett TM, Zimmer LA, Snyderman CH, Johnson JT, Raman S, et al. Head and neck malignancy: Is PET/CT more accurate than PET or CT alone? Radiology, 2005; 235: 580-6.
22. AkramAl-Ibraheem et al, Clinical Applications of FDG PET and PET/CT in Head and Neck Cancer. Journal of Oncology, 2009; Article ID 208725.
23. Tantiwongkosi B, Yu F, Kanard A, Miller FR. Role of 18F-FDG PET/CT in pre and post treatment evaluation in head and neck carcinoma. *World J Radiol*, 2014; 6(5): 177-191.
24. Schillaci O, Simonetti G Fusion imaging in nuclear medicine-- applications of dual-modality systems in oncology. Cancer Biother Radiopharm, 2004; 19: 1-10.
25. Chowdhury FU, Scarsbrook AF The role of hybrid SPECT-CT in oncology: current and emerging clinical applications. Clin Radiol, 2008; 63: 241-251.
26. Horger M, Bares R The role of single-photon emission computed tomography/computed tomography in benign and malignant bone disease. Semin Nucl Med, 2006; 36: 286-294.
27. Römer W, Nömayr A, Uder M, Bautz W, Kuwert T SPECT-guided CT for evaluating foci of increased bone metabolism classified as indeterminate on SPECT in cancer patients. J Nucl Med, 2006; 47: 1102-1106.
28. Schäfers KP, Stegger L Combined imaging of molecular function and morphology with PET/CT and SPECT/CT: image fusion and motion correction. Basic Res Cardiol, 2008; 103: 191-199.
29. Ferro-Flores G, de Murphy CA Current developments in SPECT/CT systems using 99mTc-radiopharmaceuticals. Rev Invest Clin., 2007; 59: 373-381.
30. Dumarey N, Egrise D, Blocklet D, Stallenberg B, Remimlink M, del Marmol V, et al. Imaging Infection with 18F-FDG–Labeled Leukocyte PET/CT: Initial Experience in 21 Patients. J Nucl Med, 2006; 47(4): 625-632.
31. Strobel K, Stumpe KD. PET/CT in musculoskeletal infection. Semin Musculoskelet Radiol, 2007; 11(4): 353-364.
32. Walker R, Karunasaagarar K, Lorenz E. Pyrexia of unknown origin: A review of the role of FDGPET/ CT. J Nucl Med, 2007; 48(Suppl 2): 210.
33. Takabatake D, Taira N, Aogi K, Ohsumi S, Takashima S, Inoue T, et al. Two cases of occult breast cancer in which PET-CT was helpful in identifying primary tumors. Breast Cancer, 2008; 15(2): 181-184.
34. Kumar, Rakesh et al "Role of Modern Imaging Techniques for Diagnosis of Infection in the Era of ^{18}F-Fluorodeoxyglucose Positron Emission Tomography." *Clinical Microbiology Reviews*, 2008; 21(1): 209-224. Web. 04 Oct. 2018.

35. Gudmundsson T, Torkov P and Thygesen TH. Diagnosis and Treatment of Osteomyelitis of the Jaw – A Systematic Review (2002-2015) of the Literature. J Dent & Oral Disord, 2017; 3(4): 1066.
36. Liu Y. Orthopedic surgery-related benign uptake on FDG-PET: case examples and pitfalls. Ann Nuc Med, 2009; 23(8): 701-708.
37. Gondim CFJL, Barbosa da FLM, Côrtes DR, Côrtes DR, Souza de MNLS, Leandro GE. Brain 18FFDG PET-MRI coregistration: iconographic essay. Radiol Bras, 2010; 43(3): 195-201.
38. Mallarajapatna GJ, Rastogi R. Fusion Imaging: The Current Trends. JIMSA, 2013; 26(1): 73-5.
39. Coutinho A, Fenyo-Pereira M, Dib LL, Lima EN. The role of SPECT/CT with 99mTc-MDP image fusion to diagnose temporomandibular dysfunction. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology, 2006 Feb 1; 101(2): 224-30.
40. Rastogi R, Bhargava S, Mallarajapatna GJ, Singh SK. Pictorial essay: Salivary gland imaging. Indian J Radiol Imaging, 2012; 22: 325-33.
41. Shah VN, Branstetter BF 4th. Oncocytoma of the parotid gland: A potential false-positive finding on 18F-FDG PET. AJR Am J Roentgeol, 2007; 189: W212-4.
42. Ruhlmann, V., Poeppel, T. D., Veit, J., Nagarajah, J., Umutlu, L., Hoffmann, T. K., Bockisch, A., Herrmann, K., Sauerwein, W. Diagnostic accuracy of ^{18}F-FDG PET/CT and MR imaging in patients with adenoid cystic carcinoma. *BMC cancer*, 2017; *17*(1): 887. doi:10.1186/s12885-017-3890-4.