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Ministry of Higher education and Scientific research

University of Mosul
College of Dentistry

Positron Emission Tomography (PET) Scan

A project submitted

The College of Dentistry, University of Mosul, Department of radiology in Partial Fulfillment for the Bachelor of Dental Surgery

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Certification of the Supervisor

I certify that this project entitled "The Positron Emission Tomography (PET) Scan "was prepared by the fifth-year student " Azadiene Salih Ahmed
" under my supervision at the College of Dentistry/University of Mosul in partial fulfilment of the graduation requirements for the Bachelor Degree in Dentistry.

Dr. Asmaa Basheer Rasheed

Dedication

I dedicate this work to my family, friends, and everyone who has supported me in the five years ago. especially my mother, who sacrificed everything for us, and I am proud of myself because I achieved her dream.

Acknowledgement

Thank God, above all, for giving me the strength and patience to complete my graduation research to the fullest. All thanks and appreciation to the Dean of the College of Dentistry, University of Mosul, **Dr. Rayyan Salem**, for his continued support for the college's students.

Words are not enough to describe my thanks to my research supervisor, **Dr. (Asmaa Basheer Al-saffar),** for following me up, supervising every step, and guiding me to complete the research on the subject of my field of specialization. She did not hold back anything and tolerated us until the research was completed, with all due respect, and I will never forget her.

In the end, I am indebted to my college and its professors who did not spare us a word and we entered this college as students, and thanks to them we graduated as dentists.

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List of abbreviations

PET	Positron Emission Tomograph
CT	Computed Tomography
MRI	Magnetic Resonance Imaging
FDG	Fluorodeoxyglucose
OCT	Optical Coherent Tomography
UI	Ultrasound Imaging
MRONJ	Medication-related osteonecrosis of the jaw

Introduction

Medical imaging plays a very important role in the clinical analysis and diagnosis of diseases by providing visual representations of the interior structures of a subject and/or the physiological processes hidden underneath the skin. Medical imaging also helps to establish a database with thousands of anatomical and physiological images. The emergence of these databases become a powerful tool for training both doctors and emerging machine-based systems to identify abnormalities. This resource will become more beneficial considering the significant breakthroughs developing in the fields of big data and machine learning [Giger *et al*.2018].

The field of medical imaging has employed many imaging techniques besides positron emission tomography (PET), the most notable being X-ray computed tomography (CT), magnetic resonance imaging (MRI), ultrasound imaging (UI), and optical coherent tomography (OCT) Among these imaging techniques, PET has become one of the most powerful tools to acquire functional images due to its high sensitivity to differences in the metabolic and biological activities at the molecular level .PET is currently being used in a wide variety of clinical areas, such as oncology for cancer or tumor diagnosis and staging [Roh ren *et al* 2004], neurology for Alzheimer’s disease and movement disorders [Kadir *et al* .2012], and cardiology in coronary artery disease and myocardial viability assessment [Keng et al 2004].In recent years, PET has also become an important tool in preclinical applications where animal models are used in place of humans to study disease and experiment with new drug development and treatment strategies. While animal PET imaging is mostly for small rodents, there have also been studies done on primates due to the high homology of genes with humans [Nader *et al* 2008]

Aim of the Study

1. The aim of this study is to evaluate the effectiveness of (PET) imaging in the early detection and characterization of various malignancies.
2. Assessing its impact on patient management decisions and outcomes compared to conventional imaging modalities like CT and MRI.
3. Treatment Planning and Monitoring.
4. Evaluation of Organ Function.

Chapter one
Review of literature

Positron Emission Tomography (PET) scan

PET scan is a sophisticated imaging technique that provides detailed images of metabolic and biochemical processes within the body. It involves the administration of a radiotracer—a substance that emits positrons—into the patient. As the radiotracer accumulates in areas of high metabolic activity, such as tumors or inflamed tissues, it emits gamma rays when positrons collide with electrons. These gamma rays are detected by the PET scanner, allowing for the production of images that reflect the functional state of tissues and organs. PET scans are particularly valuable in oncology for tumor detection and monitoring, in cardiology for assessing heart function, and in neurology for evaluating brain disorders [Gambhir, S. S., *et al* .2009; Chen, C., *et al* .2021]. figure 1

Figure (1): PET Scan

Table (1): PET Scan General Information

Also Known As	Positron Emission Tomography (PET)
Type	Nuclear Medicine Imaging
Purpose	Evaluate organ function and detect diseases
Preparation	Fasting, avoid strenuous activity
Fasting	Usually required
Gender	All genders
Age Group	All age groups
Procedure Duration	1-2 hours
Reporting Time	Typically within a few days
Cost	10,000 - 40,000* INR
Pregnancy Consideration	Avoided during pregnancy
Risks and Safety	Low radiation, minor risks of allergies
Accessibility	Available in specialized centers

The Main Components of a PET Scan System include:

1. The detector ring which detects gamma rays emitted by the radiotracer

2. The radiotracer itself, which is injected into the patient

3. The data acquisition system, which collects and processes gamma-ray data

4. Image reconstruction software, which converts data into 3D images

5. Display monitor, which shows the PET scan images for interpretation. [Saha, G. B. 2016]. Figure 2

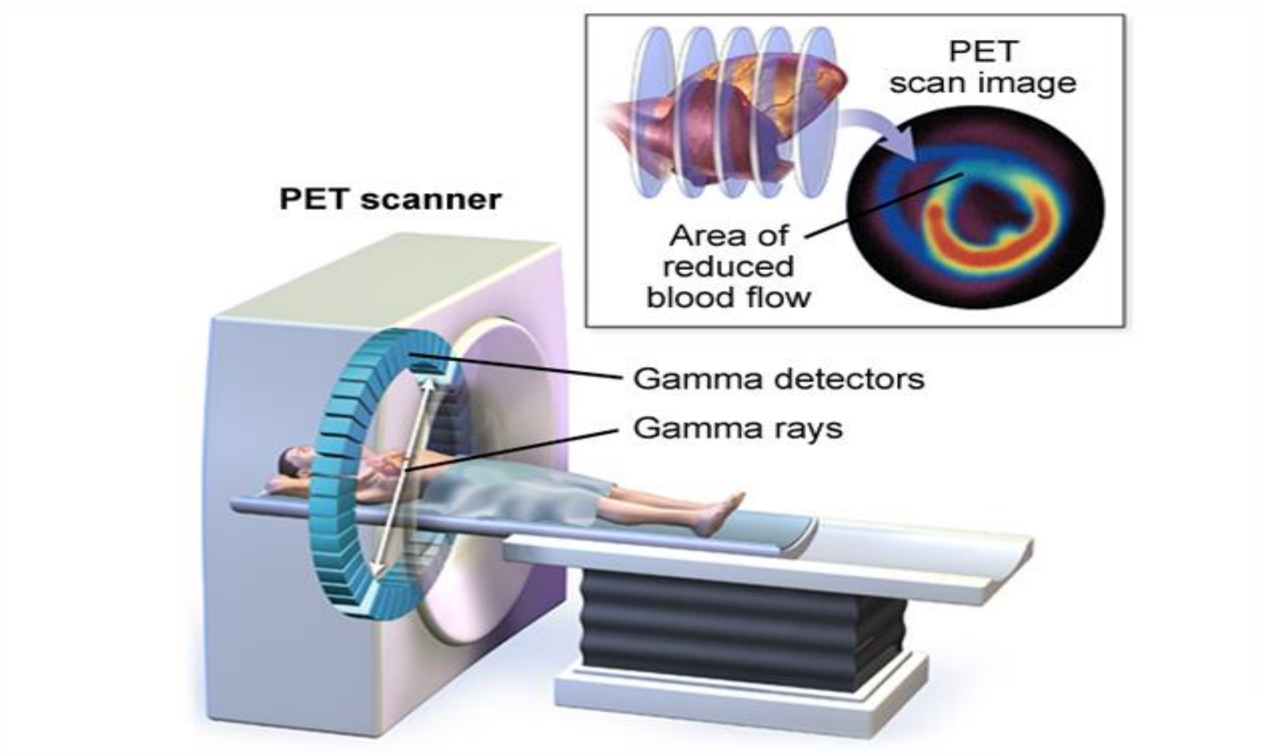

Figure (2): Component of The PET Scan

BASIC PRINCIPL

The basic principle for PET is the coincident detection of a pair of gamma rays generated from the annihilation events of the positrons from the radioactive tracer injected into a subject. The radiotracers for PET applications are analogous to common biological molecules such as glucose, peptide, and proteins, in which a radioisotope is used to substitute one of the constituents of the tracer, For example, 18F is used to replace the 16O of glucose to produce 18F-fluorodeoxyglucose (FDG), which is analogous to glucose and can indicate levels of cellular another widely used tracer is 11C-L-methionin analogous . metabolism to the amino acid, which can be used as an indicator of cancer malignancy based on the utilization of the amino acid [Saha, G.B. ng.2016; Brage *et al* 2014] . Figure 3

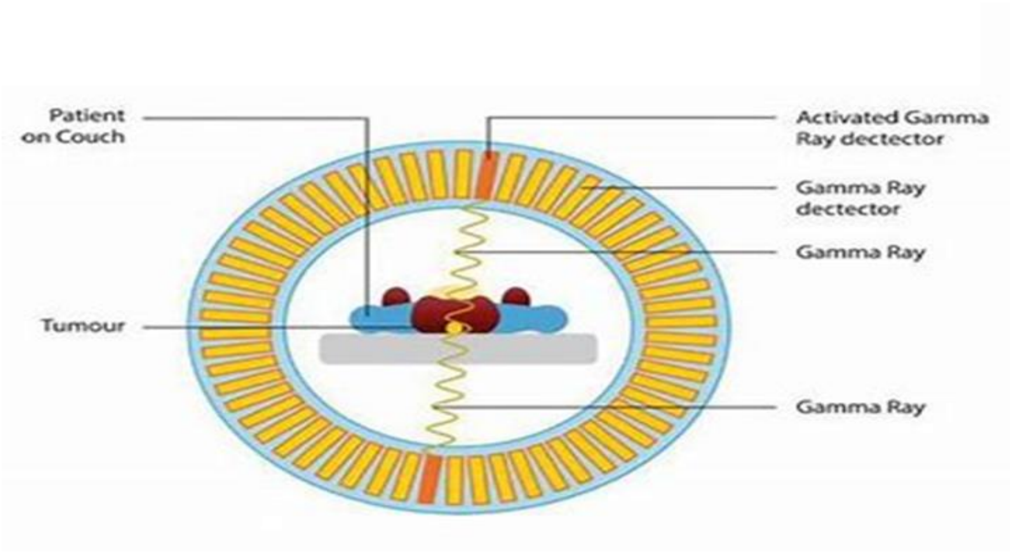

Figure (3): Positron Emission Tomography (PET) Scan

- During a PET scan, a radiotracer (a small amount of radioactive material) is injected into the patient. This tracer is typically a biologically active molecule (like glucose) that emits positrons as it decays. - The PET scanner detects these positrons, which collide with electrons in the body, resulting in the emission of gamma rays. The areas with higher metabolic activity which typically absorb more of the tracer will appear as "hot spots" on the scan [Cherry *et al* .2012]. Figure 4

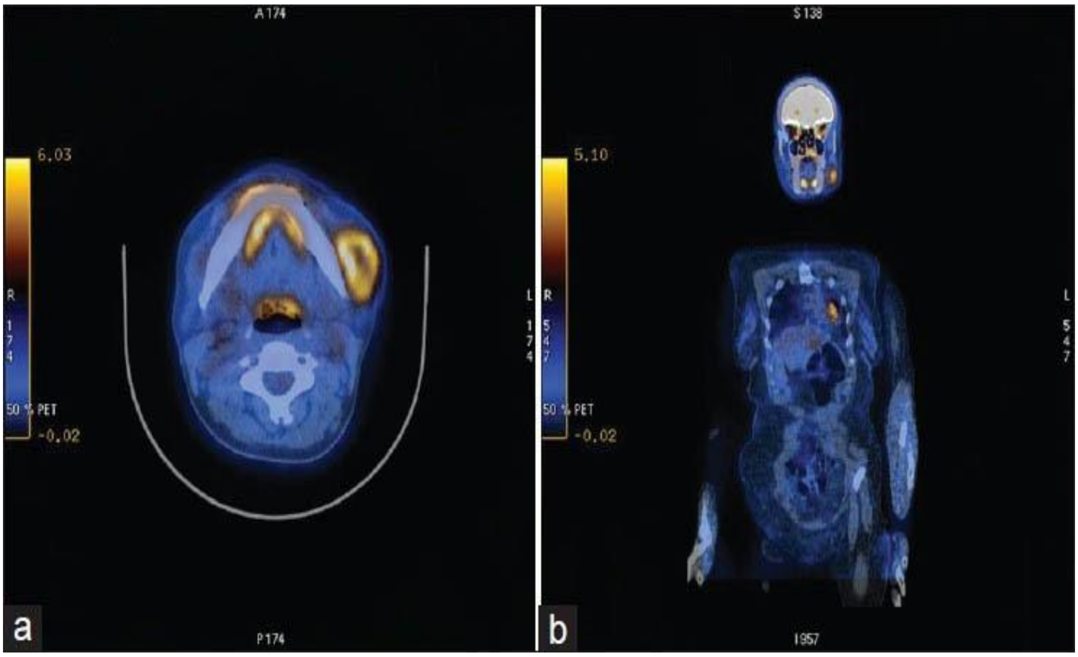

Figure (4): Positron emission tomography scan showing malignant lytic lesion of the left mandible

Functional Imaging

Unlike conventional imaging techniques that provide anatomical pictures (like CT or MRI), PET scans reveal physiological functions and metabolic processes in real time. Areas of increased tracer uptake can indicate higher metabolic activity, commonly found in cancer cells, inflammation, or other high metabolic processes [*Saha, G.B..2016*]. Figure 5

MRI CT PET Scan

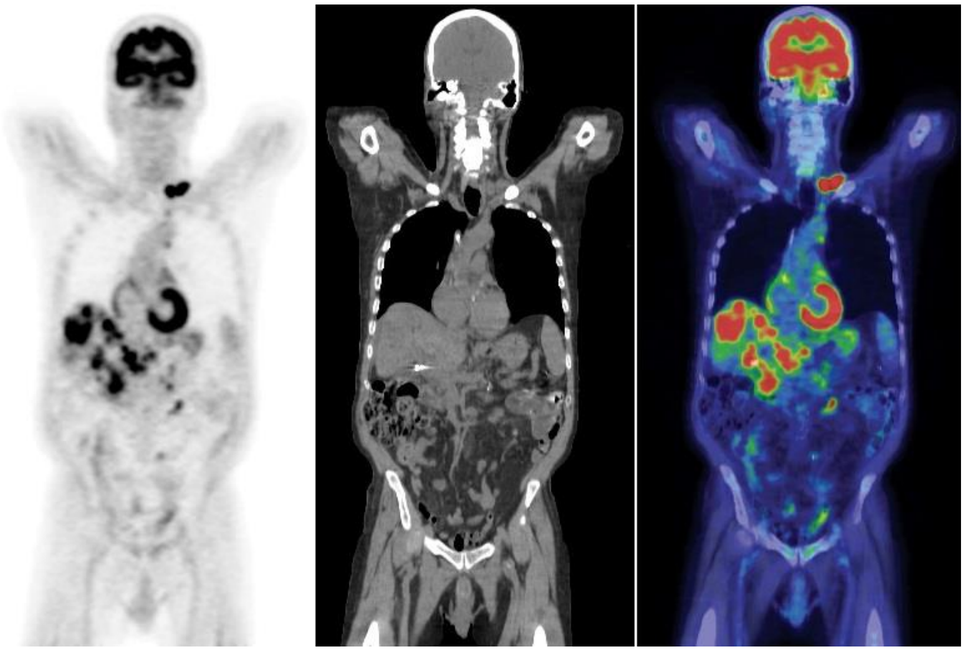

Figure (5): Differences between PET Scan ,CT and MRI

Common Types of The Radio tracer

1. **Fluorodeoxyglucose (FDG)**

   Primarily used in oncology to detect and stage cancers. FDG is a glucose analog, so it accumulates in areas of high glucose metabolism, such as tumors. It's also helpful in evaluating the response to cancer treatments [Kinahan PE *et al* .2010].

2. **Technetium-99m (Tc-99m)**

   Used in a variety of diagnostic procedures, including bone scans, cardiac perfusion imaging, and detecting malignancies. Tc-99m is versatile due to its suitable half-life (6 hours) and gamma emission, making it ideal for many applications in nuclear medicine [Kohli, M.D., & Gupta, M. 2020; Brenner, D.J., & Hall, E.J. 2007]**.**

3. **Iodine-123 (I-123)**

   Commonly used in thyroid imaging to evaluate thyroid function and detect thyroid cancers. It is also used in imaging studies of the brain and heart [Bombardieri *et al*. 2010].

4. **Gallium-68 (Ga-68)**

   Used for imaging neuroendocrine tumors, lymphomas, prostate cancer, and in research settings. Ga-68 is often used in combination with specific peptides for targeted imaging [Hofman *et al*. 2020].

5. **Fluorine-18 Sodium Fluoride (NaF-18)**

   Used for bone imaging to assess bone metastases or other bone-related conditions. It has high sensitivity for detecting early bone disease [Grant *et al*. 2008]**.**

6. **Carbon-11 (C-11) Methionine**

   Primarily used to assess brain tumors and other conditions involving amino acid metabolism, as it serves as a tracer for protein synthesis [Singhal *et al.* 2010].

7. **Oxygen-15 (O-15) Water**

   Used in research and clinical settings for measuring cerebral blood flow. O-15 water has rapid uptake and washout characteristics [Peeples *et al*.2011].

8. **Nitrogen-13 (N-13) Ammonia**

   Used in cardiac imaging to assess myocardial perfusion. N-13 allows for the evaluation of blood flow in the heart muscle [Kohli, M.D., & Gupta, M. 2020:; Brenner, D.J., & Hall, E.J. 2007].

FDG Uptake in PET Scans

Fluorodeoxyglucose (FDG) is the most commonly used radiotracer in (PET) scans, particularly for imaging various types of cancer. The uptake of FDG in PET scans provides valuable information about the metabolic activity of tissues and is a critical parameter in diagnosing, staging, and monitoring cancer [Koo, H. J., *et al.* 2016; Kohli *et al.* 2020].

Despite the chemical differences, cellular uptake of FDG is similar as for glucose. FDG passes the cellular membrane through facilitated transport mediated by the glucose transporters (GLUTs), of which more than 14 different isoforms have been identified in humans differing in their tissue distribution and affinity for glucose [Macheda *et al*. 2005].

Mechanism of FDG Uptake

According to [Koo, H. J., *et al*. 2016; Kohli, M.D., & Gupta, M. 2020"] the Mechanism of FDG Uptake include:

1. Biochemical Properties

FDG is a glucose analog that mimics glucose but has a radioactive fluorine atom substituted for a hydroxyl group. This substitution prevents FDG from being metabolized after it is taken up by cells.

Cells that have a high rate of glucose metabolism, such as cancer cells, uptake FDG more readily than normal cells because they require more energy due to their rapid growth and proliferation.

2. Metabolic Activity

Once administered intravenously, FDG is distributed throughout the body and is taken up by tissues based on their metabolic activity. The areas of higher FDG uptake typically indicate increased glucose metabolism, which can be associated with tumor activity.

3. Imaging

After a specific period, during which the FDG is allowed to accumulate in the tissues, the PET scanner detects the gamma rays emitted during the decay of the radioactive fluorine. The resulting images reveal the distribution of FDG within the body. Figure 6

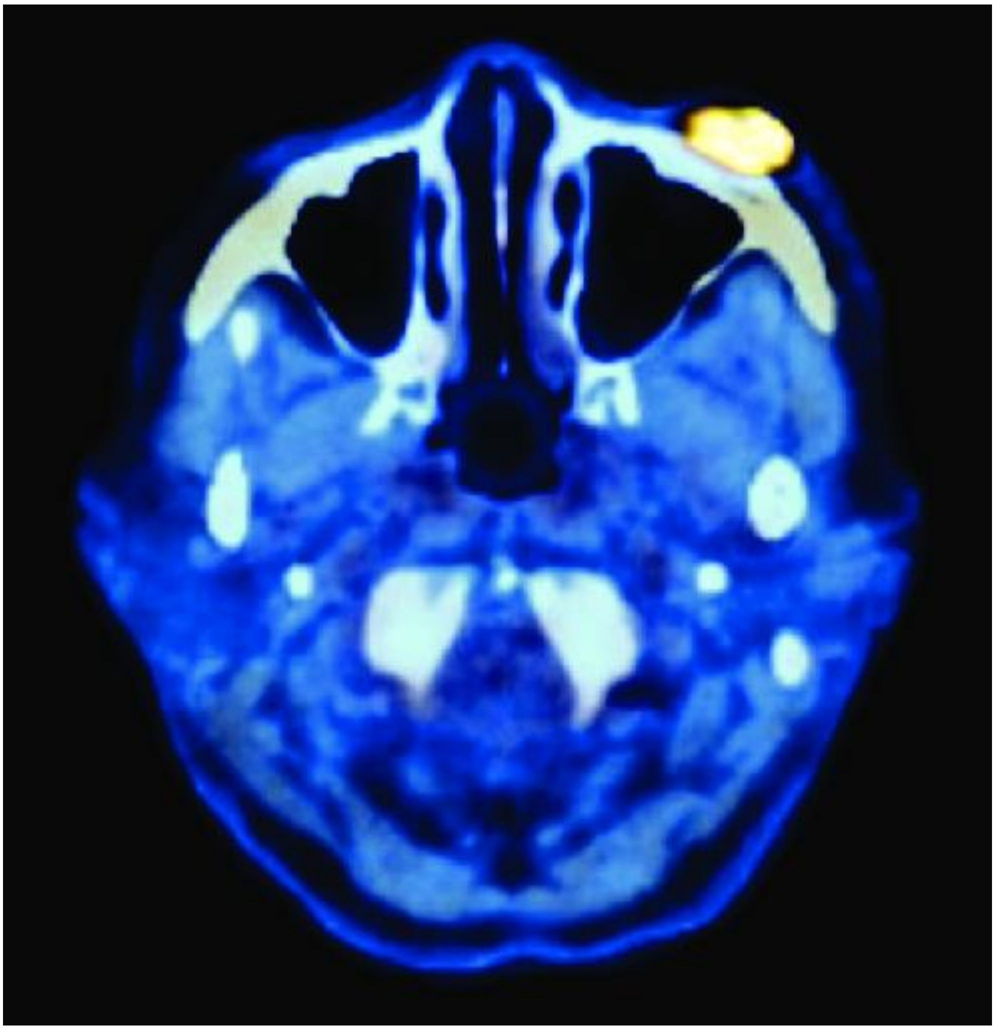

Figure (6): Positron emission tomography-computed tomography showed hypermetabolic lesion on the left cheek area

Preparation of The Patient to PET scan Procedure

- We recommend a high-protein, low-carbohydrate diet for 24 h before scanning and Alcohol and nicotine products are completely avoided for 12 h before the scan [Shankar LK, *et al.* 2006].
- We recommend complete fasting for a mini mum of 6 h before the scan, including cessation of tube feeding, dextrose-containing intravenous fluids, and parenteral hyperalimentation. During this time, only plain (unflavored) water is permitted, and there should be absolutely no sugar or carbohydrate intake of any kind, including gum, candy, or breath mints [Delbeke D, *et al*.2006].
- Routine medications may be taken, unless you have been instructed otherwise. If you are diabetic (Home blood glucose checks should be performed in the days leading to the PET exam to ensure adequate blood glucose levels (#200 mg/dL)., you may take your diabetes medication no less than 4 hours prior to the exam [Shreve P, Townsend DW, eds. .2011: Cohade C *et al*. 2010].
- patient should wear comfortable clothing and may be advised to avoid wearing jewelry or other metal objects that could interfere with scanning. Loose clothing is preferred as patients may need to lie still during the scan [Almusa H., *et al.* (2018)].
- Limit intense physical activity 24 hours prior to your exam. This includes running, heavy lifting, sports, yoga, and deep massages [Shreve P, Townsend DW, eds. 2011].

- **Pertinent Clinical Information**

A medical history should be obtained from each patient. Any history of previous treatment with radiation, chemotherapy or other experimental therapeutics, including when those therapies were performed and completed, should be documented. In particular, the use of medications that may affect the uptake or biodistribution of FDG, such as marrow-stimulating cytokines or steroids, should be noted. This information is important in assessing the interval from the completion of a certain therapy to the time of the FDG-PET study in order to ensure that all relevant confounding clinical issues are identified. Proper interpretation of PET and PET images requires a thorough understanding of the normal physiological distribution of FDG in the body, along with knowledge of frequently encountered physiological variations in FDG distribution, and recognition of non-malignant causes of FDG uptake that can be confused with a malignant neoplasm. The interpreting nuclear medicine physician should be familiar with these pitfalls. The referring physician should be aware of these factors when deciding whether and when to request a PET study and when interpreting the clinical significance of the PET findings [Vienna *et al* 2010].

- **Pregnancy**

If the examination is to be performed on a pregnant woman, the ALARA (as low as reasonably achievable) principle should be followed. The most effective ways to reduce the absorbed dose to the fetus are: (I) to encourage the woman to drink water and to void frequently after the injection of the lowest possible FDG dose (perform 3-D PET instead of 2-D); (ii) to use a 'low dose radiotracer'; and (iii) to limit the scan area so that it covers only the region of interest [Leide-svegborn *et al*. 2010].

Clinical Application of The (PET) Scans

Positron Emission Tomography (PET) scans have several important clinical applications, especially in the fields of oncology, neurology, and cardiology. PET is currently being used in a wide variety of clinical areas, such as oncology for cancer or tumor diagnosis and staging [*Roh ren, E.M.et al.2004]*, neurology for Alzheimer's disease and movement disorders [*Kadir, A.et al.*2012], and cardiology in coronary artery disease and myocardial viability assessment *[Keng, F.Y. .2004*]. One of the most prominent clinical applications of PET scans is in oncology, particularly for the detection, staging, and monitoring of cancer [*Kohli, M.D., & Gupta, M. 2020]*.

Apart from staging, PET is increasingly being used for planning radiation treatment in head and neck cancers [Ciernik *et al.*2003]. Squamous cell carcinoma is the most common cancer in the head and neck region. It is highly FDG avid and easily detected by FDG PET. PET has been found useful in localizing the site of unknown primary tumor in 25%-35% of patients with metastatic cervical lymphadenopathy [Rege link G *et al*.2002; Gould MK *et al* .2011].

Clinical Application

1. Oncology

Detection and Staging of Cancer *[Kohli, M.D., & Gupta, M. 2020]*

PET scans are widely used in the diagnosis and management of various types of cancers. The technique is particularly valuable for:

a. Identifying Metabolic Activity

PET scans can detect areas of increased metabolic activity, which is often indicative of malignant tumors. For example, cancer cells typically have higher glucose metabolism compared to normal cells, making FDG-PET scans effective for tumor identification.

b. Staging

PET imaging helps determine the extent of cancer spread (staging), which is crucial for treatment planning. It allows oncologists to visualize the tumor and assess whether there is lymphatic or distant metastasis.

c. Monitoring Treatment Response

Following treatment (such as chemotherapy or radiation therapy), PET scans can evaluate the effectiveness of the intervention by assessing changes in metabolic activity within the tumor. A decrease in FDG uptake often correlates with a positive treatment response.

2. Infection and Inflammation

- **Osteomyelitis**:

  osteomyelitis, or infection of the bone, is caused by viruses, bacteria, and fungi. The infection may be localized or may involve periosteum, cortex, marrow, and cancellous tissue. Acute hematogenous osteomyelitis is caused by seeding of organisms within the bone that are transported through the bloodstream from a remote source. Acute osteomyelitis also can be due to the spread of organisms from direct trauma, a contiguous focus of infection, and postoperative sepsis [Osman DR, *et al.* 2002].

  FDG-PET identifies active jawbone infections, especially in complex cases where CT/MRI is inconclusive, FDG is transported into cells via glucose transporters and is phosphorylated by hexokinase to 18F-2′- 18F-FDG-6 phosphate but is not metabolized further. FDG accumulates in neutrophils, macrophages, and activated lymphocytes and its uptake in these cells is related to their metabolic rate and the number of glucose transporters. Increased FDG uptake in inflammation presumably is due to several factors. There is an increased number of glucose transporters and an increased expression of these glucose transporters by activated inflammatory cells. It is important to remember that although FDG accumulates in infection, it is a nonspecific tracer that also accumulates in aseptic inflammation and malignant lesions [Love C, *et al* .2005].

- **Temporomandibular Joint (TMJ) Disorders**

PET detects inflammatory activity in TMJ arthritis [Basu, S., *et al*. 2012].

Diagnosing prosthetic joint infection with FDG-PET has been investigated extensively. in an investigation of 74 prosthetic joints, including 21 infected devices, found that the presence of increased FDG activity along the bone prosthesis interface indicated the presence of infection [Zhuang H, *et al*.2001]

3. Bone Graft and Reconstructive Surgery Assessment

PET assesses metabolic activity in bone grafts (e.g., free fibular flaps) to confirm successful integration [Kato, H., *et al.* 2015].

4. Dental Implant Planning

PET identifies regions of high osteoblastic activity to optimize implant placement. Dental implant success relies heavily on bone quality and metabolic activity. While conventional imaging (e.g., CT, cone-beam CT) assesses bone structure**,** PET scans provide functional/metabolic insights**,** enhancing preoperative planning, particularly in complex cases [Benic GI, *et al*. 2015].

5. Osteonecrosis Monitoring

Osteonecrosis of the jaw (ONJ), particularly bisphosphonate-related osteonecrosis of the jaw (BRONJ) or medication-related osteonecrosis of the jaw (MRONJ)**,** is a severe complication characterized by exposed necrotic bone in the maxillofacial region [Yamazaki Y, *et al*. 2010]. Figure7

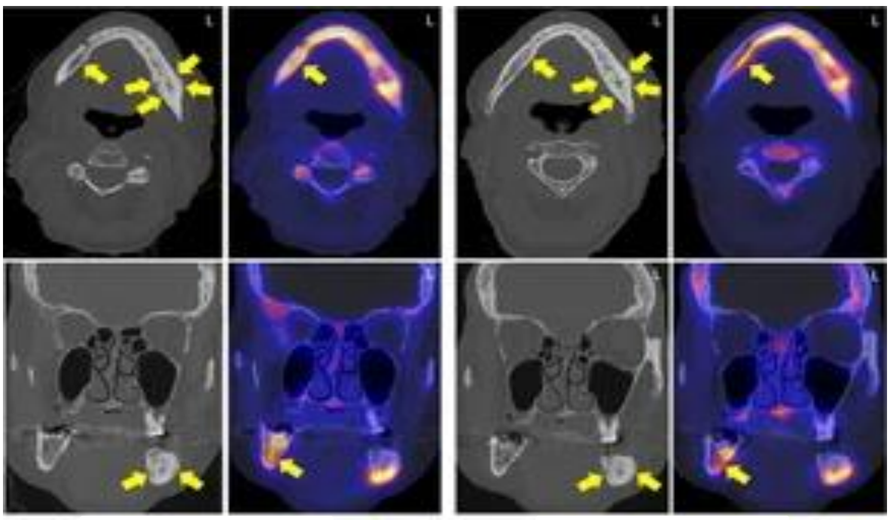

Figure (7): PET/CT image of the Medication-related osteonecrosis of the jaw

Advantage of Using a PET Scan Machine

PET scan machines offer numerous advantages in the realm of medical diagnosis and treatment. These benefits make them an invaluable tool in modern healthcare.

1. High Sensitivity for Metabolic Activity

PET scans detect metabolic changes at the cellular level, making them highly sensitive for early disease detection, particularly in cancer [Yoon, D. Y., *et al*. 2020].

2. Ability to Differentiate Between Benign and Malignant Lesions

PET scans can distinguish between benign and malignant tumors based on metabolic activity, reducing the need for invasive biopsies [Kim, S., *et al*. 2022].

3. Whole-Body Imaging Capability

PET scans can image the entire body in a single session, making them useful for detecting metastatic disease or systemic conditions [Basu, S., *et al*. 2020].

4. Combination with CT or MRI (PET-CT/PET-MRI)

Hybrid imaging techniques like PET-CT and PET-MRI combine the functional information of PET with the anatomical detail of CT or MRI, improving diagnostic accuracy [Schoder, H., *et al*. 2021].

5. **Quantitative Analysis**

PET scans provide quantitative data, such as Standardized Uptake Value (SUV), which helps in objectively assessing disease severity and treatment response [Ng, S. H., *et a*l. 2019].

6. Monitoring Treatment Response

PET scans are highly effective in monitoring the response to chemotherapy, radiation therapy, or surgery by tracking changes in metabolic activity [Wong, R. J., & Lin, D. T. 2020].

7. Accurate Staging and Restaging of Cancer

PET scans are invaluable for staging cancers, assessing lymph node involvement, and detecting distant metastases. They are also used for restaging after treatment [Burton SC, Frey K, Fahey F, *et al*.2023].

Disadvantages of PET Scans Machine

1. High Cost:

- PET scans are expensive due to the cost of the equipment, radiotracers, and specialized personnel required to operate and interpret the scans [Hicks, R. J., *et al*. 2019].

2. Limited Availability:

- PET scanners are not widely available, especially in rural or low-resource settings, due to their high cost and technical complexity [Basu, S., *et al*. 2020].

3. Limited Utility in Certain Conditions

- Poor differentiation of tumor subtypes (e.g., low-grade vs. high-grade gliomas). Limited value in organs with high baseline glucose uptake (e.g., brain, liver) [Cherry *et al*. 2017].

4. Limited Anatomical Information:

- PET scans provide functional and metabolic information but lack detailed anatomical context. This limitation is often addressed by combining PET with CT or MRI (PET-CT or PET-MRI), but this increases cost and radiation exposure [Ng, S. H., *et al.* 2019].

5. Time-Consuming Procedure:

- PET scans require significant preparation time, including the injection of radiotracers and a waiting period for tracer uptake, which can take 30–90 minutes. The scanning process itself can also be lengthy [Yoon, D. Y., et al. 2020].

6. Patient Preparation Requirements:

- Patients must fast for several hours before a PET scan to ensure accurate results, which can be inconvenient. Additionally, diabetic patients may require special preparation due to the effects of blood glucose levels on tracer uptake [Wong, R. J., & Lin, D. T. 2020].

7. False Positives and False Negatives:

- PET scans can produce false positives due to inflammation, infection, or benign tumors that also show increased metabolic activity. Conversely, small or slow-growing tumors may result in false negatives [Kim, S., *et al*. 2022].

Side Effect of The PET Scan

In general, PET scans are safe and rarely cause problems. The amount of radiation in the radioactive tracer is very low. It doesn't stay in your body for long. You should drink lots of water after a PET scan to help flush the radioactive drug from your body.

PET scans generally only pose risks in the following situations:

1. Allergic Reactions to Radiotracers:

Although rare, some patients may experience an allergic reaction to the radiotracer (e.g., fluorodeoxyglucose or FDG). Symptoms can include rash, itching, or, in very rare cases, anaphylaxis [delbeke *et al*.2006; Hicks, R. J., *et al.* 2019].

2. Radiation Exposure:

PET scans involve exposure to ionizing radiation from the radiotracer. While the dose is generally low and considered safe, repeated scans can increase cumulative radiation exposure, which may pose long-term risks [Dornfeld, 2008]

3. Discomfort or Pain at Injection Site:

The injection of the radiotracer can cause mild pain, redness, or swelling at the injection site. This is usually temporary and resolves quickly [Keng, F.Y.2004].

4. Claustrophobia or Anxiety:

Some patients may experience anxiety or claustrophobia during the scan, as they are required to lie still in a confined space for an extended period [Mazzarino, M., *et al*. (2014)].

5. Risk for Pregnant or Breastfeeding Women:

PET scans are generally avoided in pregnant women due to the potential risk of radiation exposure to the fetus. For breastfeeding women, there is a risk of radiotracer excretion in breast milk, which could affect the infant [Burton SC, Frey K, Fahey F, *et al*.2023].

6. False Positives or False Negatives:

While not a direct side effect, PET scans can sometimes produce false positives (e.g., due to inflammation or infection) or false negatives (e.g., in slow-growing tumors), which can lead to unnecessary anxiety or missed diagnoses [Graebe, m., *et al*.2010].

Chapter Tow

Conclusion

Understanding how a PET scan machine works provides valuable insights into its critical role in modern medical diagnostics. By detecting positron-emitting radioactive tracers, PET scans offer detailed images of metabolic activity and molecular functions within the body. The integration of components such as the detector ring, radiotracer, data acquisition system, image reconstruction software, and display monitor ensures precise imaging and accurate interpretation. This advanced technology aids in the detection and management of various conditions, including cancer and heart diseases, making it an indispensable tool in healthcare. As technology continues to evolve, PET scan machines will undoubtedly become even more sophisticated, further enhancing their diagnostic capabilities and improving patient outcomes.

- References

1. Giger, M.L. Machine Learning in Medical Imaging. J. Am. Coll. Radio. 2018, 15, 512–520

2. Roh ren, E.M.; Turkington, T.G.; Coleman, R.E. Clinical Applications of PET in Oncology. Radiology 2004, 231, 305–332

3. Kadir, A.; Almkvist, O.; Forsberg, A.; Wall, A.; Engler, H.; Långström, B.; Nordberg, A. Dynamic Changes in PET Amyloid and FDG Imaging at Dierent Stages of Alzheimer's Disease. Neurobiol. Aging 2012, 33, 198.e1–198.e14.

4. Saha, G.B. Basics of PET Imaging: Physics, Chemistry, and Regulations, 3rd ed.; Springer International Publishing: Cleveland, OH, .USA, 2016 .

5. Braga, L.H.C.; Gasparini, L.; Grant, L.; Henderson, R.K.; Massari, N.; Perenzoni ,M.; Stoppa, D.; Walker, R. A Fully Digital 8 x 16SiPM Array for PET Applications With Per-Pixel TDCs and Real-Time Energy Output. IEEE J. Solid-State Circuits 2014, 49, 301–314.

6. Koo, H. J., et al. (2016). "FDG PET/CT in the diagnosis of malignancy: Current applications." Clinical and Molecular Imaging, 3(1), .1-15

7. Kohli, M.D., and Gupta, M. (2020). "Current Applications of PET in Clinical Practice: An Update." Journal of the American College of Radiology, 17(8), 1032-1040

8. Brenner, D.J., and Hall, E.J. (2007). "Computed Tomography — An Increasing Source of Radiation Exposure." The New England Journal of Medicine, 357(22), 2277-2284.

9. Shankar LK, Hoffman JM, Bacharach S, et al. Consensus recommendations for the use of 18F-FDG PET as an indicator of therapeutic response in patients in National Cancer Institute Trials. J Nucl Med. 2006;47:1059–1066.

10. Delbeke D, Coleman RE, Guiberteau MJ, et al. Procedure guideline for tumor imaging with 18F-FDG PET/CT 1.0. J Nucl Med. 2006;47:885–895.

11. Shreve P, Townsend DW, eds. Clinical PET/CT in Radiology: Integrated Imaging in Oncology. New York, NY: Springer; 2011.

12. Cohade C. Altered biodistribution on FDG-PET with emphasis on brown fat and insulin effect. Semin Nucl Med. 2010;40:283–293.

13. Keng, F.Y. Clinical Applications of Positron Emission Tomography in Cardiology: A Review. Ann. Acad. Med. Singap. 2004, 33, 175–182.

14. Nader, M.A.; Czoty, P.W. Brain Imaging in Nonhuman Primates: Insights into Drug Addiction. ILAR J. 2008, 49, 89–102.

15. Gambhir, S. S., et al. (2009). "A Roadmap for the Development of PET Imaging in Oncology." Clinical Cancer Research, 15(18), 5693-5699

16. Chen, C., et al. (2021). "Applications of PET Imaging in Oncology." Frontiers in Oncology, 11, Article 682071. DOI: 10.3389/fonc.2021.682071.

17. Cherry, S.R.; Sorenson, J.A.; Phelps, M.E. Physics in Nuclear Medicine; Elsevier/Saunders: Amsterdam, The Netherlands, 2012; ISBN 9781416051985.

18. Macheda ML, Rogers S, Best JD. Molecular and cellular regulation of glucose transporter (GLUT) proteins in cancer. J Cell Physiol2005;202:654–62.

19. Valk, P. E., Bailey, D. L., Townsend, D. W., & Maisey, M. N. (2003). *Positron Emission Tomography: Basic Science and Clinical Practice*. Springer

20. Kim, S., et al. (2022). The role of PET/CT in the diagnosis and management of salivary gland disorders. Oral Diseases, 28(2), 345-353.

21. Basu, S., et al. (2020). Emerging radiotracers for PET imaging in head and neck cancer. Journal of Nuclear Medicine, 61(5), 665-671

22. Schoder, H., et al. (2021). PET/MRI in head and neck cancer: Current applications and future directions. Radiology, 298(1), 12-26.

23. Ng, S. H., et al. (2019). PET/CT in head and neck cancer: An update. European Journal of Radiology, 117, 73-85.

24. Wong, R. J., & Lin, D. T. (2020). PET/CT in head and neck cancer: Monitoring treatment response and detecting recurrence. Cancer Imaging, 20(1), 1-10.

25. Burton SC, Frey K, Fahey F, et al. Fetal dose from PET and CT in pregnant patients. *J Nuclear Med.* 2023;64(2):312-319. doi:10.2967/jnumed.122.263959 .

26. DELBEKE, D., COLEMAN, E., GUIBERTEAU, m., Procedure Guideline for Tumour Imaging with FDG-PET/CT 1.0, Society of Nuclear medicine and medical Imaging (SNMMI), Reston, VA, United States of America (2006).

27. DORNFELD, K., Post-treatment FDG-PET uptake in the supraglottic and glottic larynx correlates with decreased quality of life after chemoradiotherapy, Int. J. Radiat.. Oncol .Biol. Phys. 71 (2008) 386–392.

28. *Hicks, R. J., et al. (2019). The cost-effectiveness of PET/CT in oncology: A systematic review. European Journal of Nuclear Medicine and Molecular Imaging, 46(5), 1165-1182.*

29. *Huang, B., et al. (2021). Radiation exposure from medical imaging: A review of risks and benefits. Radiology, 298(1), 12-26.*

30. GRAEBE, m., et al., When to image carotid plaque inflammation with FDG-PET/CT, Nucl. med. Commun. 31 (2010) 773–779.

31. Mazzarino, M., et al. (2014). "Anxiety and Claustrophobia in Patients Undergoing MRI and PET Scans." The British Journal of Radiology, 87(1034), 20140564.

32. Almusa, H., et al. (2018). "Patient Attire and Artifacts: The Importance of Proper Preparation." Radiologic Technology, 89(6), 634-639 .

33. *Yoon, D. Y., et al. (2020). The role of FDG-PET/CT in the management of head and neck squamous cell carcinoma. Cancers, 12(6), 1473.*

34. LEIDE-SVEGBORN, S., Radiation exposure of patients and personnel from a PET/CT procedure with FDG, Rad. Protect. Dosim. 139 (2010) 208–213.

35. Keng, F.Y. Clinical Applications of Positron Emission Tomography in Cardiology: A Review. Ann. Acad. Med. Singap. 2004, 33, 175–182.

36. Krah, N., & Rijpkema, M. (2016). "Radionuclide Injection Site Reactions: How to Avoid and Manage." Nuclear Medicine Communications, 37(11), 1230-1235

37. Ciernik IF, Dizendorf E, Baumert BG. Radiation treatment planning with an integrated positron emission and computer tomography (PET/CT): a feasibility study. Int J Radiat Oncol Biol Phys. 2003;57:853–863. doi: 10.1016/s0360-3016(03)00346-8.

38. Regelink G, Brouwer J, De Bree R. Detection of unknown primary tumors and distant metastases in patients with cervical metastases: value of FDG PET versus conventional modalities. Eur J Nucl Mol Imaging. 2002;29:1024–1030. doi: 10.1007/s00259-002-0819-0.

39. Gould MK, Maclean CC, Kushner WG. Accuracy of positron emission tomography for diagnosis of pulmonary nodules and mass lesions: a meta-analysis. Jama. 2001;285:914–924. doi: 10.1001/jama.285.7.914.

40. INTERNATIONAL ATOMIC ENERGY AGENCY, Appropriate Use of FDG-PET for the management of Cancer Patients, IAEA Human Health Series No. 9, IAEA, Vienna (2010).

41. Grant, F. D., Fahey, F. H., Packard, A. B., Davis, R. T., Alavi, A., & Treves, S. T. (2008). Skeletal PET with 18F-Fluoride .

42. Kinahan PE, Fletcher JW. Positron emission tomography-computed tomography standardized uptake values in clinical practice and assessing response to therapy. Semin Ultrasound CT MR 2010;31:496–505.

43. Hofman, M. S., Lawrentschuk, N., Francis, R. J., Tang, C., Vela, I., Thomas, P., ... & proPSMA Study Group. (2020).

44. Singhal, T., Narayanan, T. K., Jain, V., Mukherjee, J., Mantil, J., & Chugani, H. T. (2010).

45. Bombardieri, E., Giammarile, F., Aktolun, C., Baum, R. P., Bischof Delaloye, A., Maffioli, L., ... & Chiti, A. (2010).

46.Peeples JL, Stokely MH, Michael Doster J. Thermal performance of batch boiling water targets for 18F production. Appl Radiat Isot.

47. Basu, S., et al. (2012). "FDG PET for diagnosing infection in failed prosthetic joints and osteomyelitis." *European Journal of Nuclear Medicine and Molecular Imaging*, 39(1), 65-77.

48. Kato, H., et al. (2015). "Utility of FDG-PET for evaluating bone graft viability in mandibular reconstruction." *International Journal of Oral and Maxillofacial Surgery*, 44(8), 938-943.

49. Benic GI, Elmasry M, Hämmerle CHF. Novel digital imaging techniques to assess the outcome in oral rehabilitation with dental implants: a narrative review. Clin Oral Implants Res. 2015;26:86 96

50. Yamazaki Y, Kitagawa Y, Hata H, Abe T, Murai C, Shiga T, et al. Use of FDG PET to evaluate hyperbaric oxygen therapy for bisphosphonate-related osteonecrosis of the jaw. Clin Nucl Med 2010;35(8):590–1.

51. Osman DR: Diagnosis and management of musculoskeletal infection. In: Fitzgerald RH, Haufer H, Malkani RL, (eds): Orthopedics. St. Louis, Mosby; 2002, pp. 695-707

52**.** Love C, Tomas MB, Tronco GG, et al: Imaging infection and inflammation with 18F-FDG-PET. RadioGraphics 2005;25:1357-1368

53. Zhuang H, Duarte PS, Pourdehnad M, et al: The promising role of 18F-FDG PET in detecting infected lower limb prosthesis implants. J Nucl Med 2001;42:44-48