PET-CT Physics, Instrumentation, and Techniques

2

2.1 Introduction

The PET-CT is an important imaging modality of molecular imaging. The molecular imaging is defined as the visualization, characterization, and measurement of biological processes at the molecular and cellular levels by the SNM, i.e., Society of Nuclear Medicine and Molecular Imaging [1]. This PET-CT is an important component of hybrid imaging which means a combination of functional and structural imaging for quantification [2, 3]. This imaging modality quantification is done based on the amount of radiotracer uptake in a particular tissue over a period of time. Thus, FDG PET-CT has revolutionized modern medicine with the newer concept of personalized medicine. The PET-CT is widely used in various pathologies on oncology, neurology, cardiology, infection inflammation, and various newer miscellaneous applications [4, 5]. Thus, PET-CT has now been established as an important multidisciplinary imaging modality. PET-CT is being used widely for the evaluation of the malignancies especially for diagnosis, staging and restaging, monitoring response to therapy, and for indications like Radiotherapy planning. PET-CT has also become the important modality for imaging in animal models also to study the various disease pathologies, new drug developments, and various treatment strategies [6]. Thus, PET-CT offers a wide range of information to study the biological and biochemical processes.

PET alone as the functional imaging modality is not specific as the exact location of the anatomical structures needs to be defined. For this fusion of PET with CT or MRI is done and PET-CT/PET-MR is formed by the co-registration of the functional and anatomical images. This is called as Hybrid Imaging.

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2.2 Principle of PET-CT

2.2.1 Annihilations

PET is based on the basic principle of annihilation process in which the photons are released when the radionuclides emit positrons, and they undergo the annihilation with the electrons [7]. The radiotracer injected is analogous to the common biological molecules present in the body like glucose, peptides, and proteins in the body. These released photons are emitting the energies of 511 keV at exactly opposite to each other [8]. This energy is identified by coincidence imaging by the detectors. This is based on the law of the conservation of energy where the 511-keV represents the energy equivalent of the mass of the electron. In this process of the bombardment of the target material with photons which will be accelerated in the cyclotron for the production of the positron-emitting radionuclides. This forms the basis of the radionuclide production [9].

2.2.2 Radiotracer Techniques

In order to detect the gamma rays due to annihilations, scintillation crystals [10] are used to absorb and convert the high energy gamma rays into low energy photons. With the development of the detector technology lot of limitations of PET are not seen now. The commonly used detectors are Lutetium-Oxyorthosilicate LSO which has remarkably high density, high light output, fast decay time, and excellent resolution. In this process photosensor like PMT, APD, or SiPM is used to convert the light signal into the electrical signal [11]. The amount of PET uptake is directly proportional to the amount of glycolysis in the FDG Radiotracer. The positrons emitted from a radionuclide have enough kinetic energy to travel.

Thus, a lot of factors are important in the sequence of technical, patient-related factors then biokinetics of radiotracer distribution. The amount of physiological uptake and the pathological uptakes.

Evolution of PET was documented in 1934 when Irene and Curie proved the formation of radioactive materials, which decayed by emitting the positrons. The first medical Cyclotron was established by Lawrence to produce the Isotopes [12, 13].

The basic component of PET is made up of multiple ring detection systems consisting of Bismuth germinate oxide (DGO) [14] and cesium fluoride. PET instrumentation is developed parallelly along with the development of radiochemistry. Many compounds like ^{15}O, ^{13}N, ^{11}C, and ^{18}F. Thus, dedicated PET-CT was introduced commercially with the evolution of instrumentation and radiochemical diversity.

2.3 PET Physics

2.3.1 Positron Emission

Positron is a positively charged electron with the same mass of an electron. This positron annihilates with electrons to form photons moving in the opposite direction. Now this annihilation process forms the basis of the PET. Positron emission is based on the isobaric decay process, which is also known as Beta plus decay [15]. In this process, the radionuclides are converted into neutron with release of positron. This positron decay results in the conversion of one isotope into another. In this process of annihilation where the energy is emitted in opposite directions at 180° to each other and can be detected by PET detectors. The most commonly used detectors are LSO (Lutetium Oxyortho Silicate). With the advent of detector development, a lot of new techniques are coming. One technique is TOF (Time of Flight) (Diagrams 2.1 and 2.2).

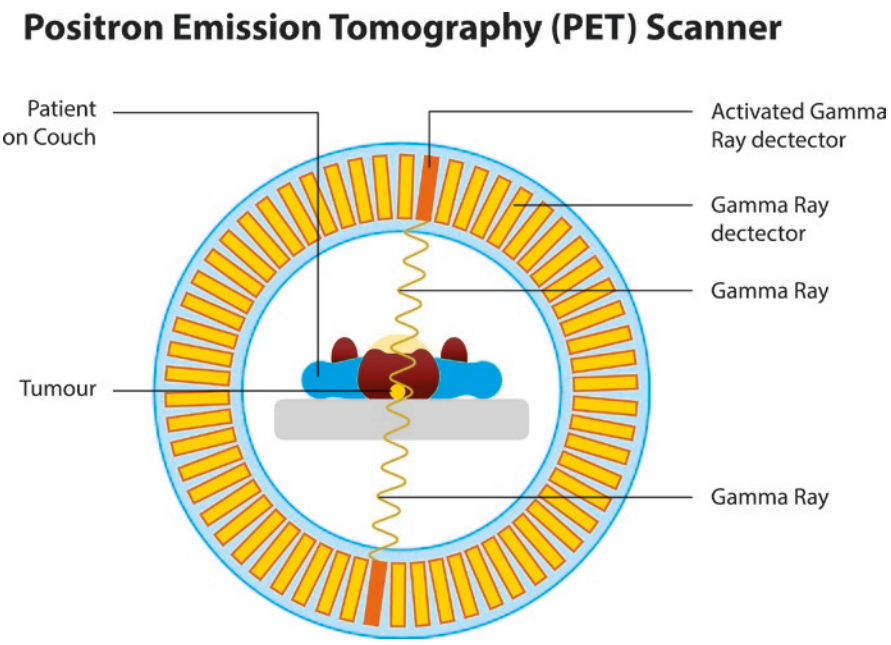

Diagram 2.1 PET-CT gantry showing PET scintillators showing the photon energy being detected at 180° to each other on the basis of the Einstein's principle. This forms the basis of the PET image acquisition

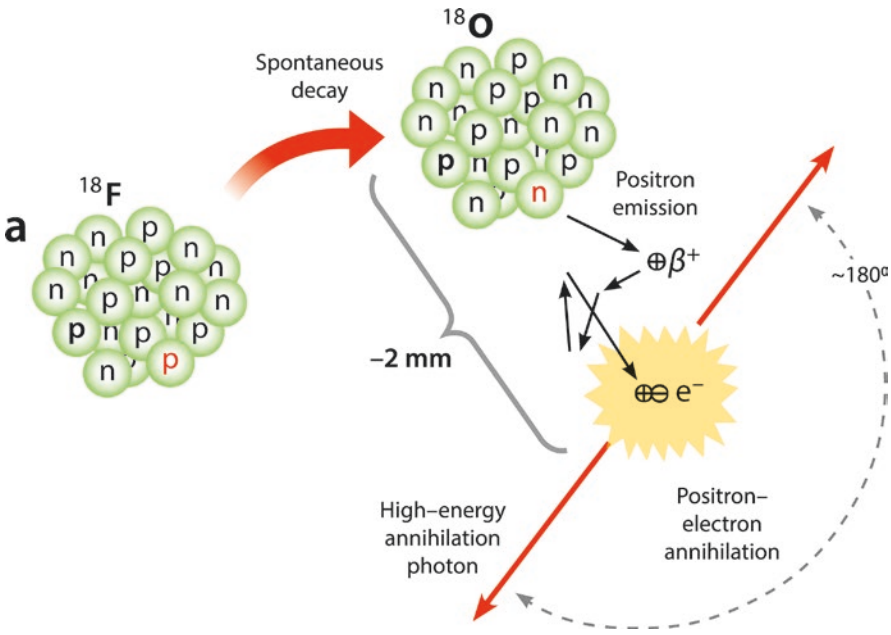

Diagram 2.2 This is the process of positron electron annihilation where the energy released on the basis of the Einstein's principle at 180° to each other which is detected by scintillators

2.3.2 PET Scanner

PET scanners are made up of multiple small detectors that are arranged adjacent to each other and typically the diameter range is from 60 to 90 cm. Around 25,000 detectors are seen in the length of 10–25 cm. PET detectors are high-density scintillator crystals which has a capacity to converts the photon energy. These scintillators are combined to a device known as photomultiplier tube (PMT) [16]. In this process, light is converted into electric signals. These signals from each detector are combined in the coincidence circuit (Diagram 2.3).

2.3.3 PET Image

Thus, PET images are formed by the single voxel images, which are calibrated with the radioactive tracers. Thus, the 511-keV energy from different annihilation processes is clubbed together for the image formation. In this PET-CT, CT has a significant role in attenuation correction. With the advent of technology, a lot of new developments have occurred in PET-CT, one of them is TOF PET.

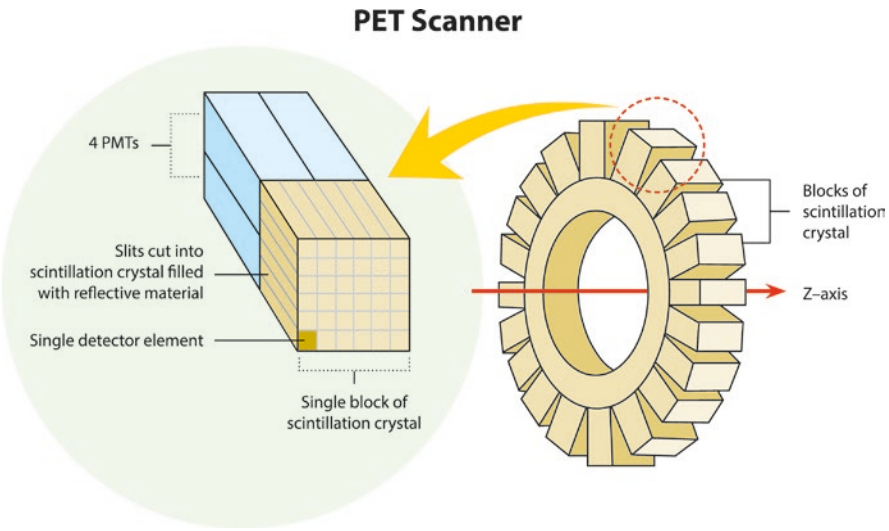

Diagram 2.3 Blocks made up of scintillation crystals with Photomultiplier tubes

2.4 Radiotracers

Many radiotracers are there for the imaging of PET, but the ideal radiotracer depends on the half-life. This half-life for the imaging should be in imaging limits and feasibility, so that it should be injected and transferred in the body and scan should be done in shorter time frames [17]. The shorter half-life of a couple of minutes and a longer half-life in many hours and days are not recommended for imaging. The ideal radiotracer in PET imaging should be comfortable to inject and scan should be done at the same go. These radiotracers are prepared by the synthesis process in Cyclotron [18]. Radiotracer is produced after a couple of reactions. The most commonly used radiotracer is Fluorinateddeoxyglucose (F-FDG). F-18 is being produced in cyclotron by bombarding the O-18 enriched water with high energy protons. Negatively charged hydrogen ions are accelerated in cyclotron forming the positive hydrogen ions that are high energy and directed toward O-18 enriched water. This proton undergoes the nuclear reaction with O-18 forming F-18. The synthesis of the FDG is done from the F-18 component. Thus, the FDG produced is a sterile, pyrogenic, colorless, and clear liquid. This F-FDG is glucose which is tagged with the radioactive material. In this process, the radioactive purity is greater than 95%. The concept of this glucose metabolisms glycolysis which is also known as the Warburg effect [19]. The amount of cellular uptake of FDG is directly proportional to the activity in a particular tissue or an organ. This biochemical process of FDG formation depends on the glucose transporters (GLUT) pathway. Thus, FDG uptake is not only specific for cancer but all other applications like infection and inflammation where there is an increased turnover of the glucose. F-FDG is avid for many pathologies and not sensitive to the diagnosis for all these pathologies. For this many new radiotracers are been invented, which are more organ specific or system specific and can be used easily for the diagnosis. This is becoming the basis of personalized medicine in future (Diagrams 2.4 and 2.5).

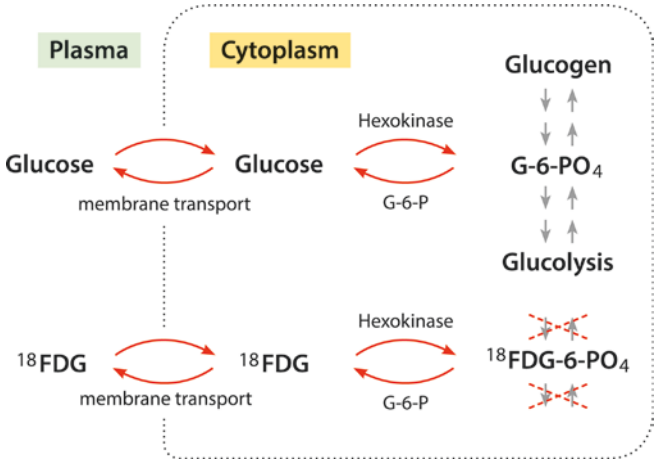

Diagram 2.4 Comparison of the normal glucose and fluorodeoxyglucose metabolism

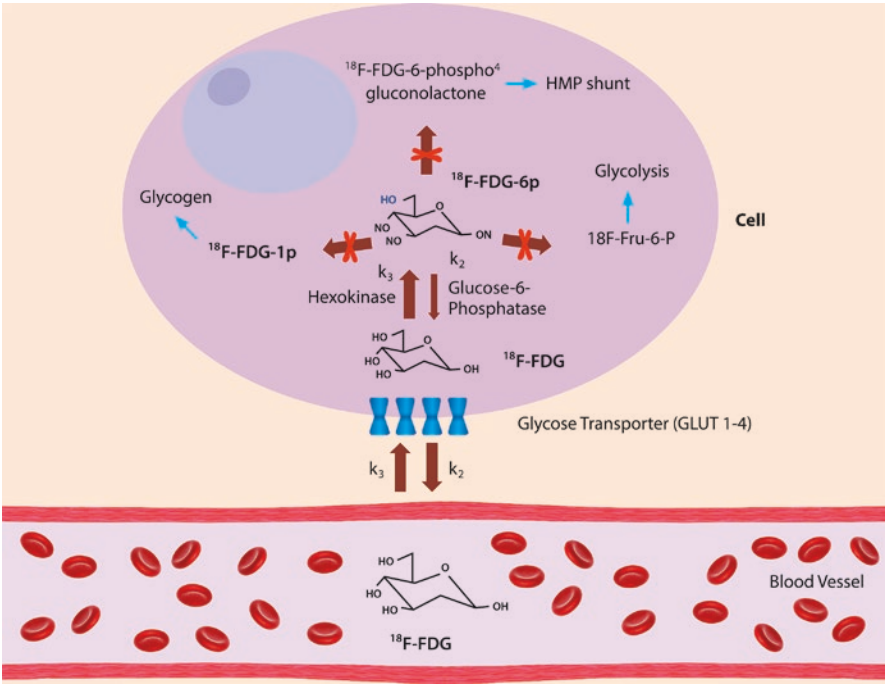

Diagram 2.5 Glucose metabolism within the cell and the role of GLUT1, GLUT2, GLUT3 and GLUT 4

2.5 Factors Influencing FDG Uptake

The malignant cells have important properties of rapid proliferation, increase in size local invasion and distant metastases. The amount of the FDG radiotracer uptake depends on the various factors like the number of tumor cells, grading of tumor, histological subtype, and vascularity. The vascularity of the tumor is related to the amount of oxygen in a particular tissue with less oxygen, this entity is known as tumor hypoxia [20] (Diagrams 2.6 and 2.7).

This is the same principle of the PET in infection and inflammation. Sometimes it becomes difficult to differentiate between different pathologies as many of them will have same amount of uptake. Here some criteria are there to differentiate between them but still a few cases a little difficult. For this, the advancements in the radiotracers are also there where in the future it will be more focused to evaluate pathologies in relation to the radiotracer pathologies (Diagram 2.8).

The amount of FDG uptake in a particular tissue whether physiological or pathological depends on the amount of the uptake, which is quantified by standardized uptake values (SUV) [21].

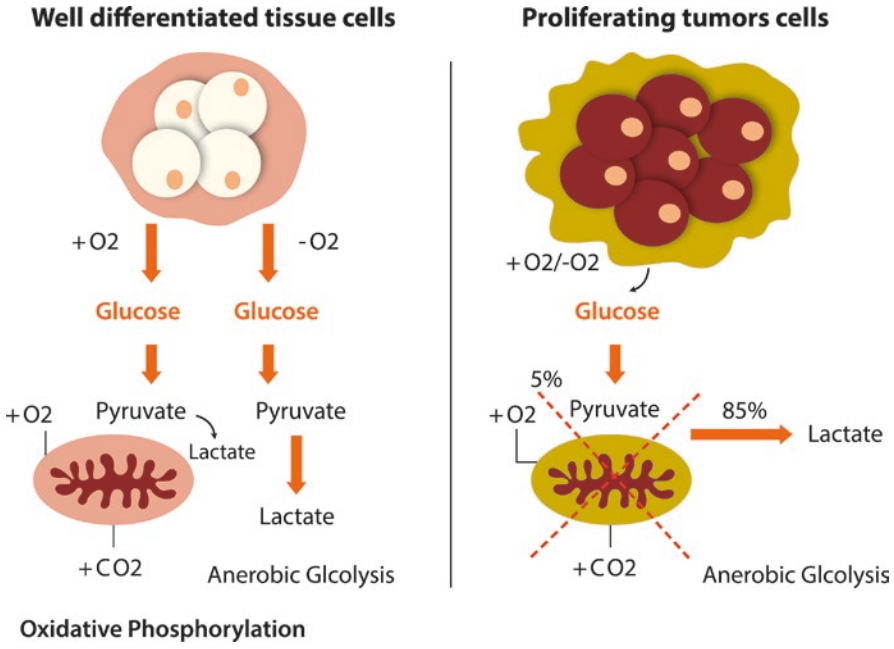

Diagram 2.6 Glucose metabolism in normal tissues and tumor tissues. In normal tissues, the oxidative phosphorylation takes place while in tumor proliferating cells it does not take place

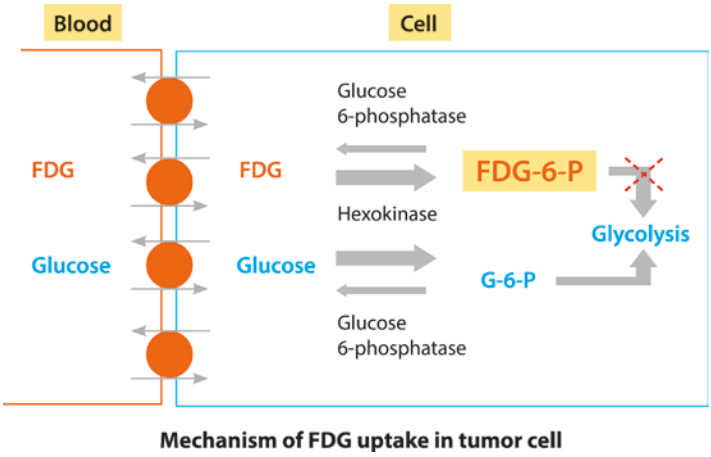

Diagram 2.7 Metabolism of FDG in tumor cells, the FDG 6 phosphate to glycolysis does not take place

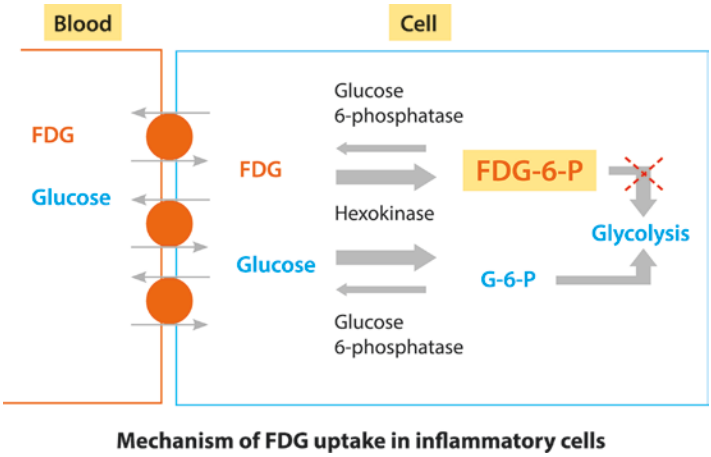

Diagram 2.8 Metabolism of FDG in inflammatory cells. The FDG 6 Phosphate to glycolysis does not take place. Thus, the mechanism of metabolism is same in both the processes

2.6 PET-CT Scanning Technique

2.6.1 Patient Preparation

Fasting for 4–6 h is needed before the PET-CT scan. This is the optimal duration needed for the optimum uptake in pathological tissues. To avoid caffeinated and alcoholic beverages. The amount of uptake depends on glucose metabolism in a particular tissue. It is important to know the knowledge of the distribution,

physiologic uptake, and common normal variants [22]. False increased or decreased blood glucose levels needs to be quantified. The ideal blood sugar level should be below 150 mg/dl. The blood sugar levels at higher levels, above 200 mg/dl, should be rescheduled. The blood sugar levels between 150 and 200 mg/dl [23] should be administered insulin to reduce the blood sugar levels. False-positive results can be seen in insulin-induced hypoglycemia. The average dose of FDG uptake is 10 mCi which is injected intravenously. No obvious contraindications for FDG injection are there. Ideally scan is done after 60 min of the FDG injection. The ideal position is arms up position this is needed to reduce the beam hardening artifacts while doing CT. The various protocols of whole-body imaging are there, base of the skull to mid-thigh is the standard and most widely used protocol practiced throughout the world. Limited PET-CT scans are usually done for cardiac, neurological applications, and prosthetic joint infections imaging. Upper and lower limbs scan to be done separately along with the whole-body scan. This again depends on the indications like melanoma or any specific clinical symptoms in the upper or lower limb.

2.6.2 CT Technique

As per the sequence of events in PET-CT, CT is done first followed by PET. Different protocols are being used for CT, that is, plain CT, single phase study, or triphasic study depending on the organs involved [24]. Triphasic CECT is planned in cases of neuroendocrine tumors, hemangioma liver, etc. This planning is an integral part of PET-CT planning. This CT imaging is done in the proper inspiratory phase. Lung window acquisition to be done separately after whole-body scan to delineate the lungs. If needed HRCT to be done separately.

2.6.3 PET Technique

After the CT is over PET is done. In whole body, the different bed positions vary from six to seven beds, but this varies depending on the height of the patient. Each bed position will have overlap due to the concept of misregistration between the CT and PET. Each bed position varies from 11 to 15 mm [25].

Once the PET is over then delayed images of CT abdomen are taking to evaluate the bowel loops, Urinary bladder, and pelvic pathologies.

2.7 Image Interpretation

PET images depict the amount of radiotracer uptake in particular tissue, which is basically the concentration of the radiotracer uptake. These are the uncorrected images which have to be converted to the corrected images. This has to be done by the CT data which is used to convert uncorrected images to corrected images. This attenuation correction is being done by the 511-keV photons that are passing

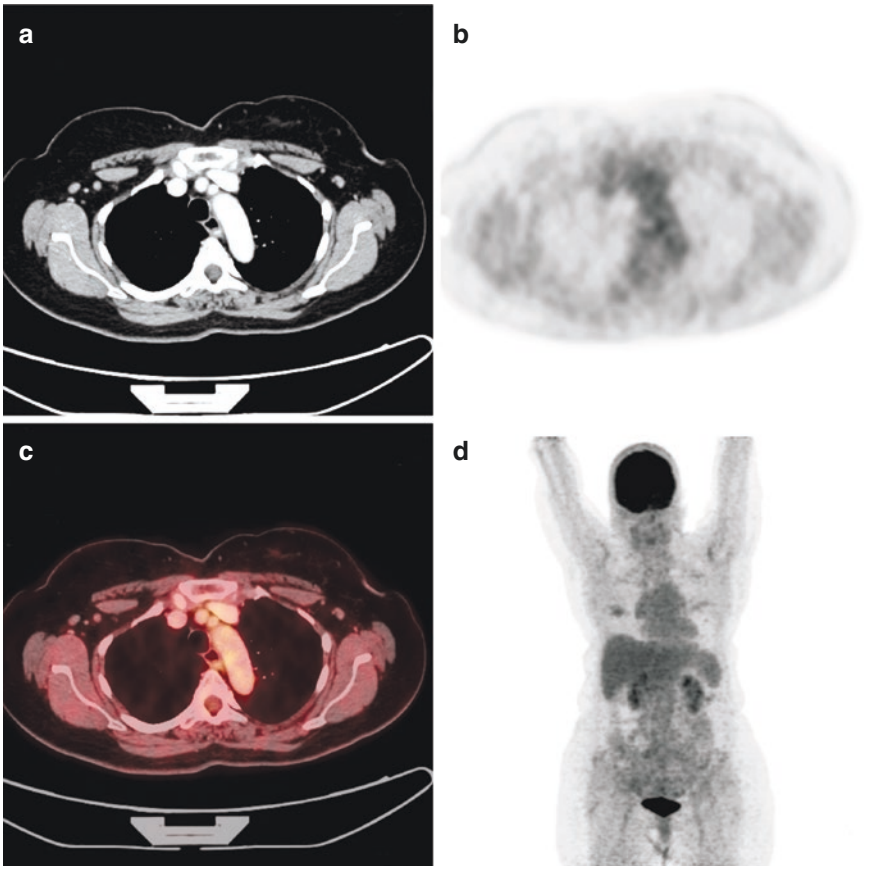

Fig. 2.1 Normal whole-body PET-CT scan from vertex of the skull to midthigh showing no abnormal physiological uptake. Normal physiological uptake seen in the renal pelvicalyceal system and urinary bladder

through the patient. Finally, corrected images of PET are ready. These fused images are reconstructed into Axial, Sagittal, and Coronal images (Figs. 2.1 and 2.2).

The different criteria for the assessment of the radiotracer uptake are done by visual inspection of SUV max and glucose metabolic rate. The most widely used are SUV max, which is semi-quantification for the amount of FDG uptake.

The normal physiological uptake is seen in the muscles and fat [26, 27]. Increased physiologic uptake is also seen in the brain and heart, especially more prominently seen in the cortex and basal ganglia in the brain. The uptake in the myocardium is based on the cardiac activity which appears normal and physiologic in the majority of whole-body scans. Dedicated cardiac scans are also done with FDG and other radiotracers. Mild uptake is also seen in the liver, spleen, and bone marrow, which can be physiological, systemic inflammation, and post-chemotherapy stages.

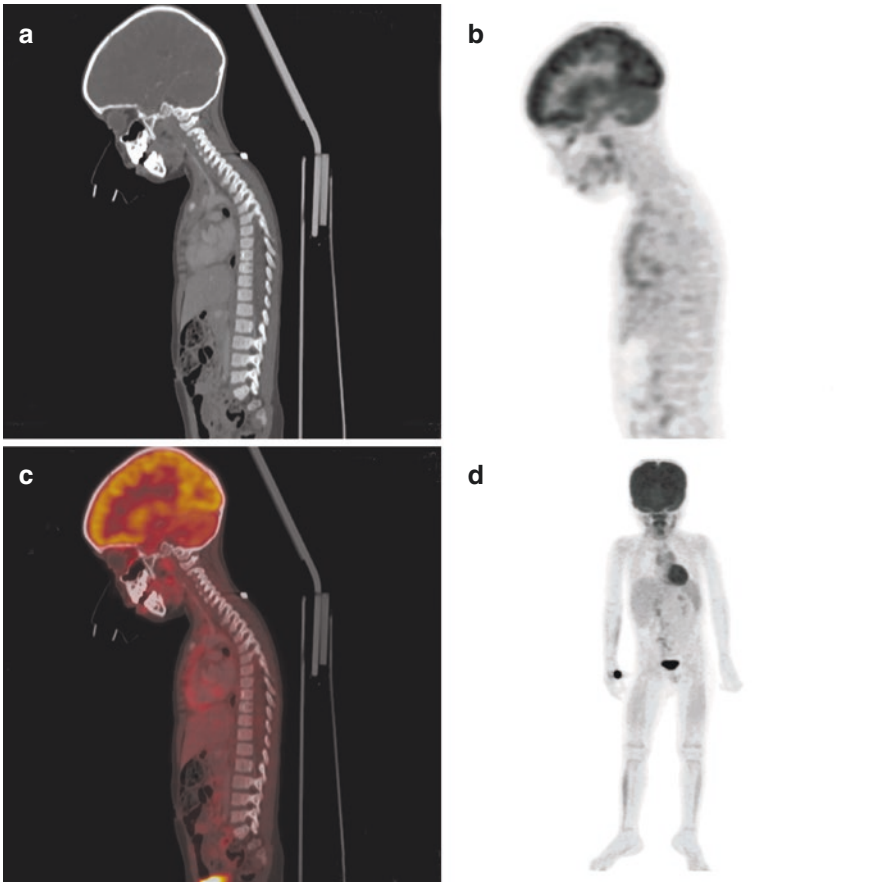

Fig. 2.2 Normal whole-body PET-CT scan from vertex of skull to feet. This is possible in the pediatric age group as examining PET-CT machine table is of sufficient height. Normal physiological uptake seen in the brain parenchyma, nasopharynx, cardia, and urinary bladder

Skeletal muscle uptake is also an important source of error, especially in cases where the patient is not resting or any involuntary activity is there (Fig. 2.3).

Physiological increase in FDG activity is also seen in the pelvicalyceal system of kidney and urinary bladder because FDG is excreted by the urinary system. Physiologic uptake also noted in the thyroid gland and GI tract. This physiologic uptake is highly variable which can be diffuse or focal can be seen in the all segments of the bowel, but most commonly seen in the caecum and recto-sigmoid junction. The role of CT with oral contrast in the bowel is more helpful, especially in relation to the mucosal or submucosal lesion, which can be malignant or premalignant. The SUV is a semiquantitative assessment of the radiotracer uptake from the static single point in the time PET image. The tissue tracer activity is in microcuries per gram, injected radiotracer dose in millicuries, and patient weight in

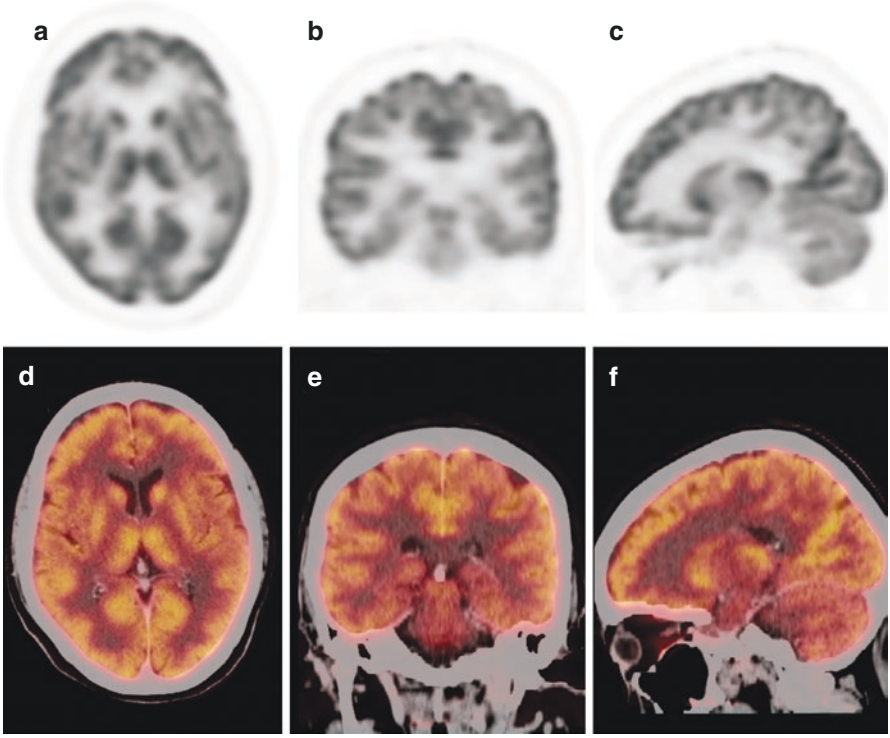

Fig. 2.3 Normal brain PET-CT uptake seen in the cerebral parenchyma. Cortex shows more uptake than the gray matter

kilograms. SUV of the tissue is documented as minimum, maximum, or mean in the region of interest (Figs. 2.4 and 2.5).

$$\text{SUV} = \frac{\text{Tracer activity in tissue}}{\text{Injected radiotracer dose / Patient weight}}$$

The tissue tracer activity is in microcuries per gram injected radiotracer dose is in millicuries per gram, injected radiotracer is in millicuries and patient weight is in kilograms.

The SUV values are quantified as minimum, maximum, and mean. The mean SUV is the mathematical mean of all the values. The minimum and maximum SUV max are the lowest and highest SUV max values. Ideally, the SUV max values are ranging from 0.5 to 2.5. Some of the literature mentions 2.5–3.0 and above SUV is consistent with the malignancy. But a lot of variations are there in this. It is better to have less radiotracer uptake. Variations are also seen in this which can be quantified or optimized [28].

With this, it is important to set a protocol for standardized SUV values.

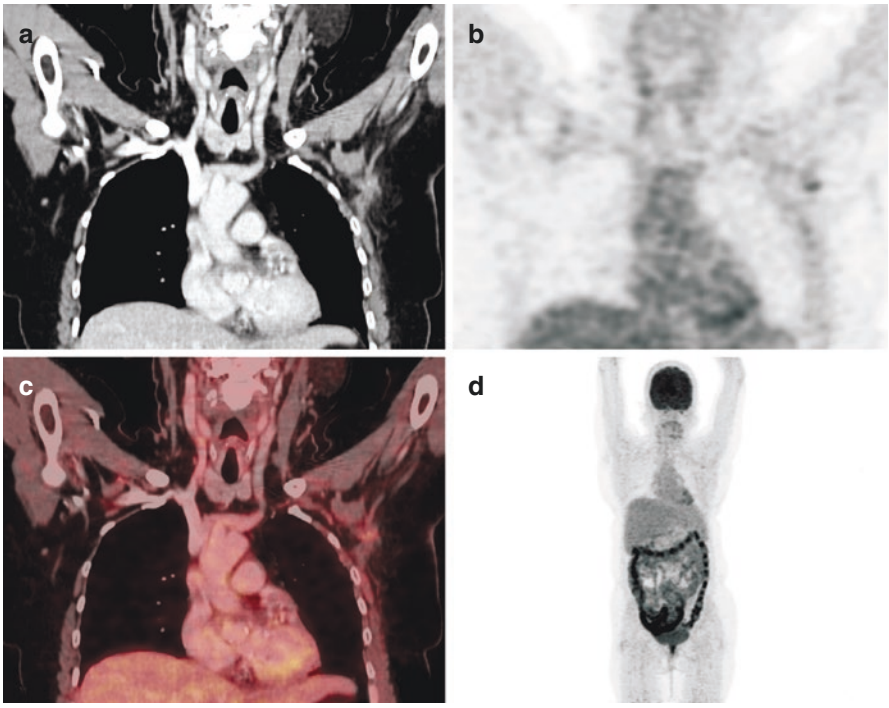

Fig. 2.4 Normal whole-body PET-CT scan with physiological uptake in the distal ileal loops and entire colon. This physiological uptake has to be differentiated from the pathological uptake in the bowel loops

Some of the studies we need to use special protocols like in the Head and Neck lesions Puff cheek technique is commonly used. This helps in the evaluation of the in situ lesions in buccal regions (Fig. 2.6). The other protocols like administration of the Lasix for the proper urinary bladder distension for small focal lesions or mild subtle urinary bladder wall thickening. Rectal contrast for the well distension of the anorectal, rectal, and sigmoid colon lesions. This is crucial for the well delineation of the focal, mild wall thickenings.

2.8 Limitations and Artifacts of PET-CT

Patient motion is the commonest cause of the artifacts. Proper PET and CT co-registration have to be done which is mostly based on the spatial resolution of the radiotracer activity and the attenuation correction. CT artifacts also caused by metallic artifacts and prosthesis, etc. will cause a lot of attenuation correction artifacts [29, 30]. Some other artifacts like significant activity before or after injecting the FDG.

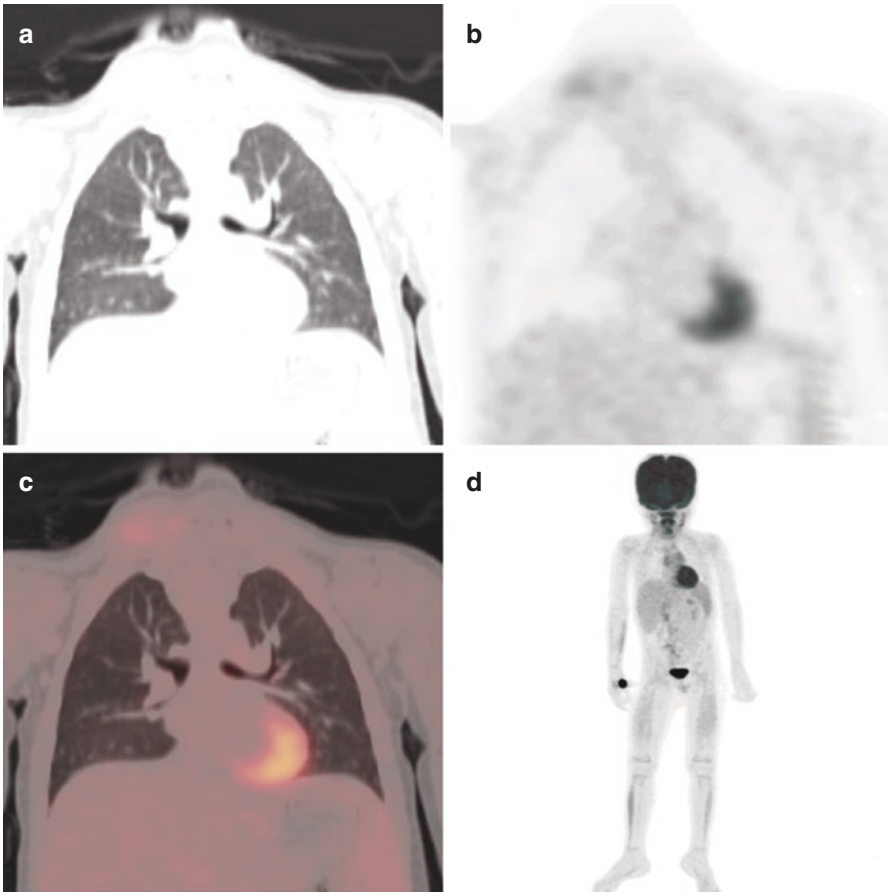

Fig. 2.5 Whole-body PET-CT scan of pediatric age group. Lung fields appear normal. Site of the injection of radiotracer seen at the right wrist joint. Normal physiological uptake seen in cerebral parenchyma, nasopharynx, cardia, and urinary bladder

Normal uptake should not be confused with physiologic uptake in kidney, brain, bowel, cardia, liver, and other organs.

2.9 Advantages of PET-CT

PET-CT is helpful in accurate localization of small radiotracer uptakes, distinguishing the normal and abnormal disease activities.

PET-CT combined imaging modality provides excellent functional information from PET and spatial and contrast resolution of the CT [31, 32].

PET-CT attenuation correction for quantitative or semiquantitative assessment of data which can be done by CT.

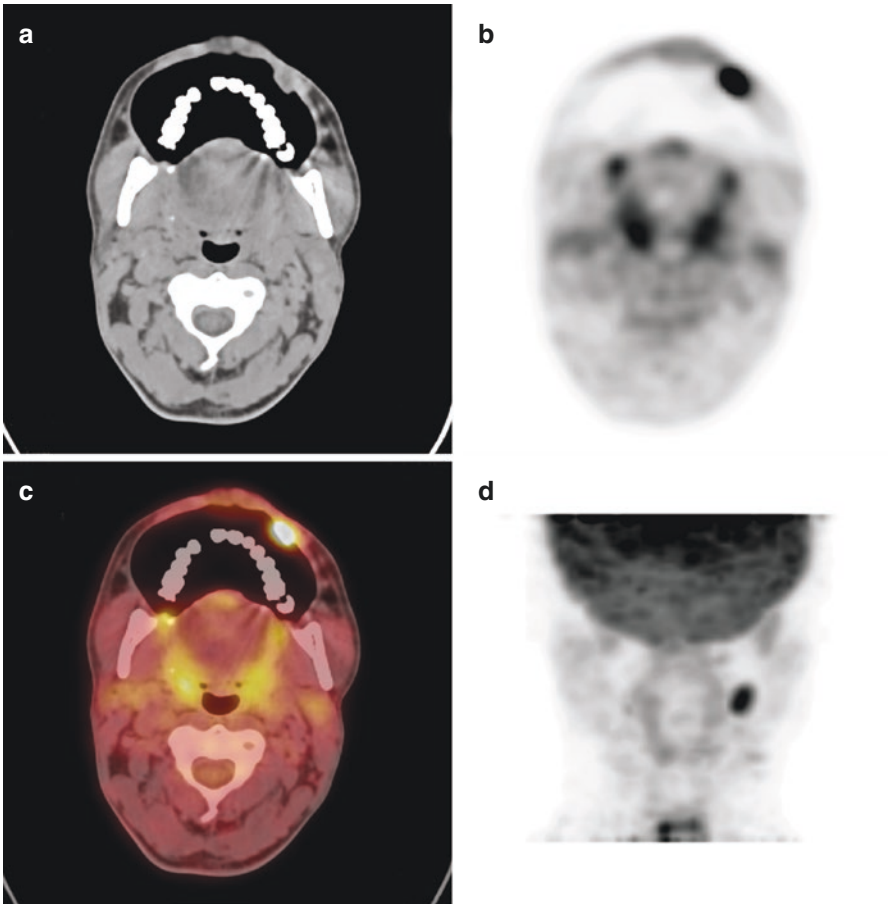

Fig. 2.6 Puff cheek technique is the specific technique that is helpful in differentiating the small subtle lesions and in situ lesions of buccal mucosa and also involving the gingivobuccal sulcus and retromolar trigone. Here in this small nodular lesion seen in the left buccal region is more clearly seen and shows significant uptake. This clarity of this lesion would be not precise if done in routine protocol

2.10 Conclusion

Thus, PET-CT is an important imaging modality, which has evolved in a significant way for imaging. The basis of the detection of the coincidence photons during annihilation, accurate co-registration of the quantitative and functional information with CT is the hallmark of the PET-CT imaging. Patient preparation, data acquisition, data reconstruction, and image interpretation are crucial to the high-quality PET-CT imaging. With many newer radiotracers and applications, it is the modality of choice in many conditions.

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