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Time-of-flight Techniques role in the survival Breast Cancer using Hybrid PET/CT Imaging

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ABSTRACT

Positron emission computed tomography (PET) has significant role in oncology field. Commonly used in the purpose of evaluation and management including tumor diagnosis, staging, restaging and monitoring patient response after therapy. It has the ability in the evaluation and detection of the metabolic activity in targeted tissue inside human body. This often achieved by using radiopharmaceutical ^{18}F-Fluorodeoxyglucose (FDG).The annihilation reaction occurred between both electron and positron which end up with 511 keV pair photons emitted and recorded using special conventional block detectors based on Lu_2SiO_5:Ce (LSO) and $Bi_4Ge_3O_{12}$ (BGO) scintillators which has a special characteristics in terms of crystal absorption efficiency, density, light yield , spatial and time resolution. The aim of this study is to identify the effects of time of flight (ToF) and partial volume effect (PVE) as quantitative imaging parameters in the early detection of breast cancer in Eastern province using 18-FDG as metabolic imaging radiotracer and PET/CT mCT flow Scanner. A literature review was conducted to understand the role of image processing parameters in the oncology imaging cases specially breast cancer using PET/CT machines. Publish med, Google Scholar and Nuclear medicine Journal were the research original source.

Keywords: ^{18}F-FDG, time of flight, partial volume effect, breast cancer.

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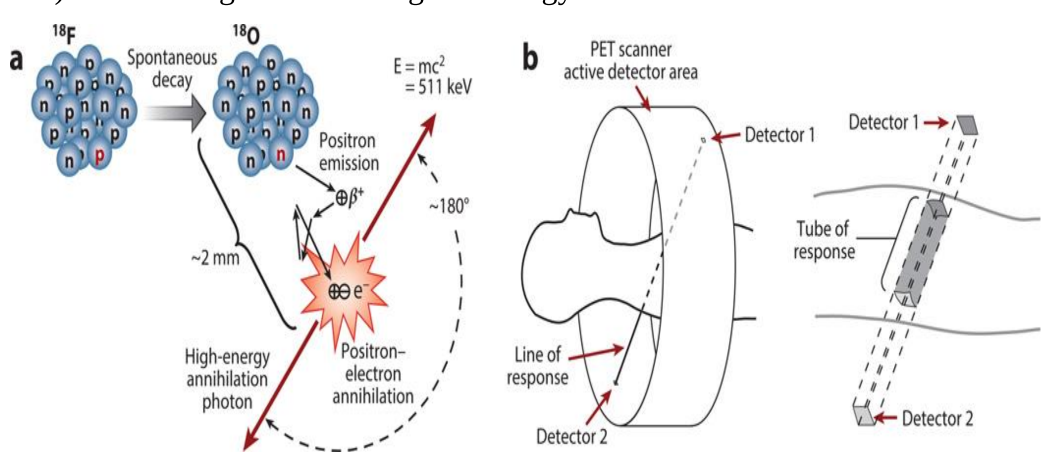
INTRODUCTION

Early diagnosis of breast cancer greatly increases the chance of cure and survival from the disease. The mammogram is widely used for early detection of breast cancer, but its effectiveness and accuracy have been a concern for a long time as well as its inability in detecting small cancers, especially in women with dense breast tissues. Therefore, it is an unmet clinical need to develop a simple, convenient test to overcome the shortcomings of mammography. Positron Emission Tomography-Magnetic Resonance Imaging (PET-MRI), Positron Emission Tomography-Computed Tomography (PET-CT), and Single Photon Emission Computed Tomography-Computed Tomography (SPECT-CT) are classified as the state of art modalities in Hybrid Imaging. It plays a significant role in providing morphological and functional imaging findings in a single examination that 18F helps in clinical oncological fields [1].

PET-CT is one of the unique medical imaging modalities. It plays a significant role in the early diagnosis of different types of disease like breast cancer, cardiovascular and neurological disorders, infection and inflammatory diseases. Moreover, it has a powerful role in oncology, especially in staging and restaging numerous cancer diseases that support treatment plan as well as monitoring the patient responses to the treatment given and roll out any suspected recurrence [2]. Positron interaction detects a pair of gamma (γ-rays), which are emitted from the radionuclide introduced into the human body. In PET images, malignant tumors are characterized by increased glucose metabolism compared with normal cells, producing a good contrast between cancerous and normal cells. Also, it provides information about the chemical functions inside organs and tissues. CT image is added to improve image enhancement, attenuation correction and reducing noise ratio [3, 4]. PET/CT consists of two merged ring detectors, one for CT that provide excellent attenuation correction and the other detector for PET that consists of different types of powerful crystals like LSO and BGO, multi- detectors arranged circularly supported with Photomultiplier tubes (PMTs) that have significant timing and energy resolution [5, 9].



Time-of-flight (TOF) and Partial Volume Effect (PVE) became the primary application in PET/CT machines. In the 1980s, the initial development occurred in two-dimensional (2D) modes with limited sensitivity and spatial resolution. Later, analytic image reconstruction methods were used, leading to more efficiency using LSO crystal, a three-dimensional (3D) mode with high sensitivity and high spatial resolution parameters that reduced scan time duration and the signal to noise ratio (SNR) improvement reconstruction in obese cancerous patients. [5]. Partial Volume Effect (PVE) is highly dependent on several parameters like the tumor metabolic rate uptake, size, and shape. It can measure the maximum Standardized Uptake Value (SUV max) uptake accurately, quickly, and in reality which helps in the determination of cancer treatment effectiveness [6,7]. PET allows the visualization and quantification of tumor features on a molecular level beyond the morphological extent shown by conventional imaging such as tumor metabolism or receptor expression. The tumor metabolism or receptor expression information data derived from PET which can be used as tool for visualization of tumor extent, for assessing response during and after therapy [8]. Breast cancer is the second cancer death cause worldwide. There are many types of breast cancer which can be presented in different site of the chest wall and the breast body such as the lobular, ductal as well as the surrounding tissue in between. Breast cancer can be categorized in three main groups: invasive, non-invasive and metastatic. The breast cancer with all its types and subtypes are carried out multi complex environmental, and genetic factors. Breast lesion imaging investigation include both self and clinical breast examination then mammography and ultrasound guided biopsy. In addition, MRI, PET/CT, SPECT/CT are providing efficient and complementary diagnostic information [12-14].

MATERIALS AND METHOD

PET/CT as instrumentation model

Molecular and biochemical imaging offering several advantages using unique machine-like PET/CT. The physics of detection and emission the coincident photons expressing the unique capabilities in PET design. [10, 14, 25]. The basic principle behind positron imaging is simply obtained when the annihilation reaction between positron and electron occurred resulting of antiparallel 511 KeV photons emitted then detected and recorded by simultaneously using special scanner as shown in Fig. 1. In turn, this determined by variable constants like scintillator type. The state of art in this machine model concentrating in the modulation and combination between two rings detectors of both PET and CT in one gantry. This detector of internal machine component including the set of block detectors arranged in ring shape surrounding the field of view which support image spatial resolution, high energy experiments of high effect and light yield of inorganic scintillation crystal [5, 15, 16, 17]. The patient is placed inside the gantry surrounded by a ring of detectors that define the scanner's active sensor area. When two annihilation photons are detected within a few nanoseconds of each other, the two points of interaction define a line of response. [2, 14, 17]. The coincidence events in PET categorized into four major events in every PET machine random, scatter, true, and multiple events as shown in Figure 2. The key of PET imaging identified when the Line of Response (LOR) of the true coincidence photons detected by two detector elements, the total number detected is mainly proportional to radioactive tracer amount used in the tube response. The role of TOF shown in Figure 3 and Figure 4 measuring the time differences of the annihilated photoelectrons along the LOR.[16-17-20]. To achieve the best high spatial resolution accuracy, set of detectors array adjusted using very sensitive vacuumed photo multiplayer tubes attached to block detectors. [20, 23, 24].

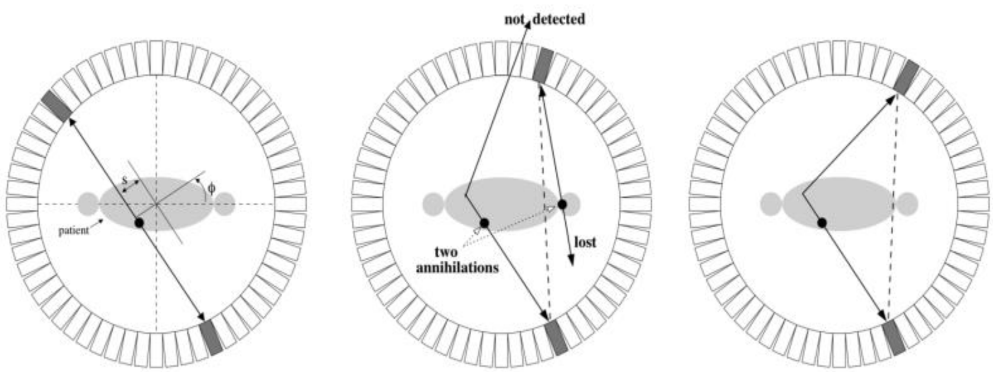


Figure 2: Explain the types of coincident events. From left to right: True coincidence, random (accidental) coincidence and scattered coincidence. In the last two types, the annihilation event (marked with a black circle) does not lie on the apparent line of response between the two photon detections.

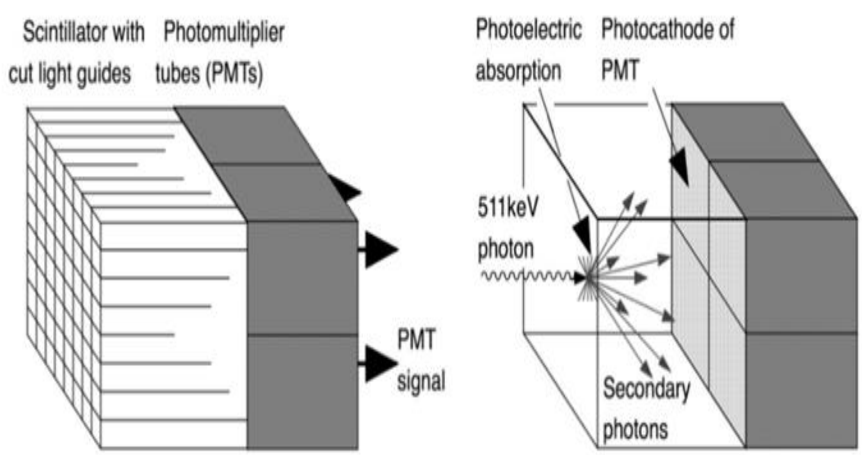


Figure 3: Schematic of a block detector with finely segmented scintillator crystals read out by four photo-multiplier tubes.

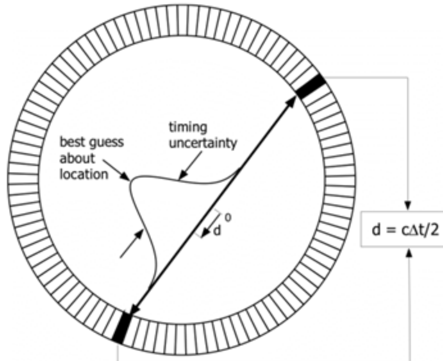


Figure 4: Coincidence processing in time-of-flight (TOF) PET data acquisition. The combination of TOF and LYSO properties increase both of time resolution and stability.

Table 1: The most common scintillation crystals used in PET model

	Crystal Material	Cost	Light output	Effective Density	Decay Time
1	NaI (Tl)	Cheaper	Highest	Lowest	Long
2	BGO	Expensive	Lowest	Highest	Long
3	LSO(LYSO)	More expensive	High	High	Very short
4	GSO	More expensive	Very high	Lower than LSO	Very short

PET/CT Patient Preparation

Patient preparation for a whole-body PET scan using radioactive glucose analogue 18F-FDG include special preparation for both diabetic and non-diabetic patients. It is recommended that patient blood glucose level must be lower than 11 mmol/L, if the sugar level out of this range the study must be excluded. The patient should be injected in dark, quiet waiting area and must be kept warm for 60-120 min post injection. Moreover, explain the procedure to the patient before injecting to reduce radiation exposure and apply As Low As Reasonably Achievable (ALARA) concept. The bladder must be empty prior to the scan time. The assigned technologist must insure and followed the patient imaging and preparation protocols as recommended to avoid the repetition of the procedure [9].

Table 2: Patient preparation of Whole Body PET/CT using 18F-FDG

Parameters	Diabetic	Non- Diabetic
Blood Glucose Level IV Cannula	Blood glucose level 120-180 mg/dl not exceed 200.	
Fasting Period	4-6 hrs. prior to 18F-FDG injection	
Medication	Insulin or metformin must be taken 6 hrs. prior to the study with light breakfast.	Pain killer if needed Eluthroxin or concor is acceptable
Post-Operative Surgery	(6-8 weeks) Depends on the surgical site	
Special Diet	Low carbohydrate diet two days prior the study water allowed	Low carbohydrate two days prior to the study and water is allowed
Exercise	Not allowed 48 hrs. prior the scan (Muscle uptake)	
Medical Imaging & Histopathology	If WC, schedule the PET for the following day Biopsy: 7-14 days before PET/CT	

Work Data Flow in PET and Image Reconstruction

PET scanner consists of multi circular ring detector, The protocol starting with the scout view as well as the CT aligned with PET images, CT provide the entire organs morphological details and used as attenuation correction step point of PET. The result appears in the screen as fused image. The acquisition time varies according to specific parameters like the patient body weight (BMI) and administered activity, 2D versus 3D image, the count rate capability and PET/CT scanner sensitivity. The data acquired in 2D form are corrected, converted, reconstructed and stored as 3D images form data. During reconstruction the image look like noisy it can be normalized and smoothed using mathematical filter back projection (FBP) and ordered-subsets expectation maximization (OSME) algorithm techniques. Figure 5 [19, 20, 23]. Partial volume effect (PVE) can be lowered by properly modeling the point spread function (PSF) either in reconstruction or in post reconstruction. List-mode TOF reconstruction can lower PVE and benefit clinical PET imaging with better image resolution and controlled noise, which could increase lesion detectability and better diagnosis accuracy [17, 18, 23-25].

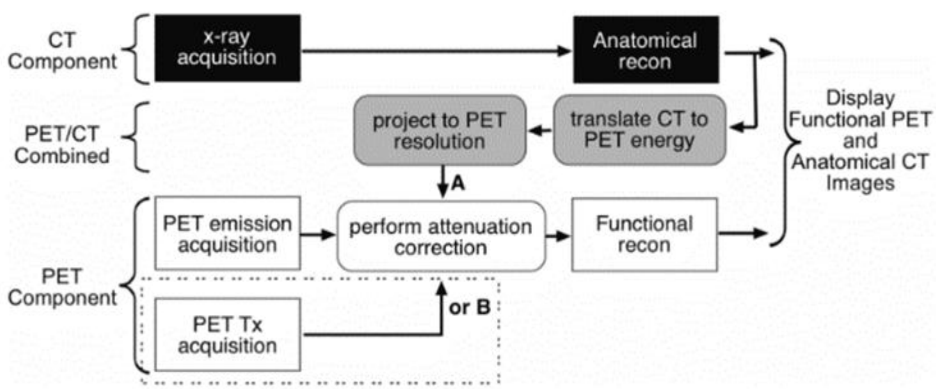


Figure 5: Data flow in PET/CT scanner. NB: Reconstruction= (Emission-Random)/(Attenuation)/Efficiency

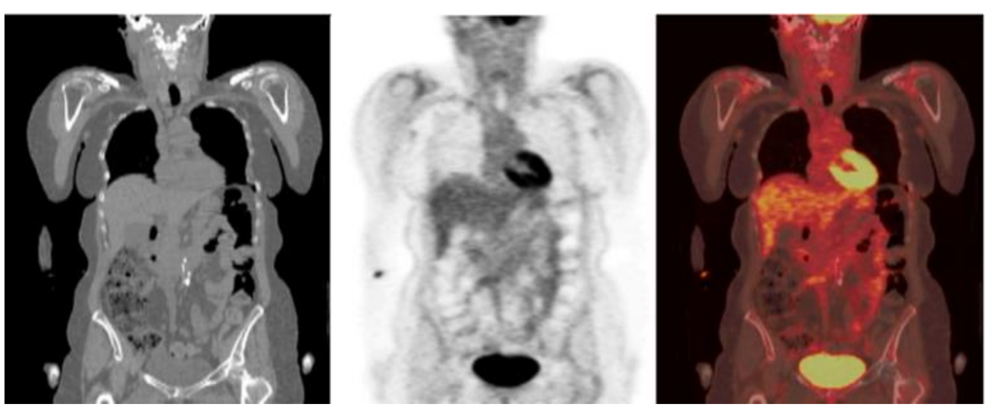


Figure 6: Normal Bio distribution of PET/CT image using ^{18}F-FDG radio isotope mCt-Flow PET Fused WB PET/CT scan.

TOF Vs NON-TOF concept in accepting and rejecting image blur and tumor detection

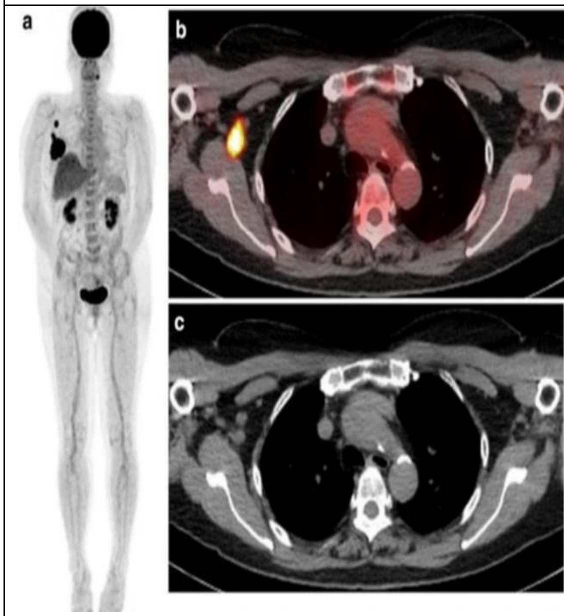
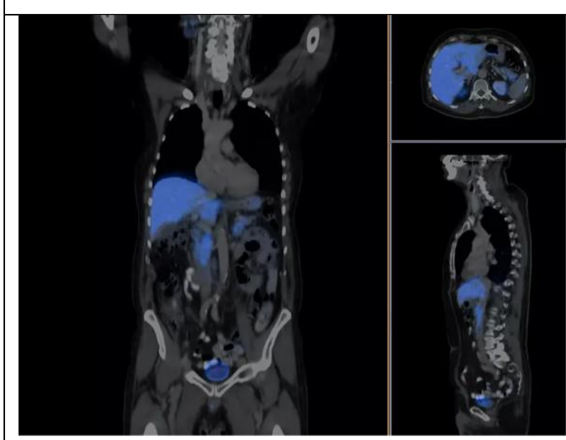
Image Details	Comment
	**Image a** Maximum intensity projection of the FDG-PET image showing intense uptake points in the right breast and ipsilateral axillary fossa. **Image b** PET/CT and image **c** the CT portion. The images showed abnormal FDG uptake corresponding to two metastatic ipsilateral axillary nodes 7 and 8 mm in shortest diameter. Suggesting the absence of nodal cancer spread. However, histopathological specimen of the dissected axillary lymph node revealed extensive cancer involvement.
Figure 7: PET/CT IDC – BC.	

Image Details	Comment
	Philips manufacturer using TOF technique in hybrid imaging of cancer which definitely improving the image contrast, SNR as well as the point of spread function by 30% compared into NON TOF image method to rule out the lesion enhancement and blurring the small outer lesion.
Figure (8). TOF PET-CT imaging (Philips).	

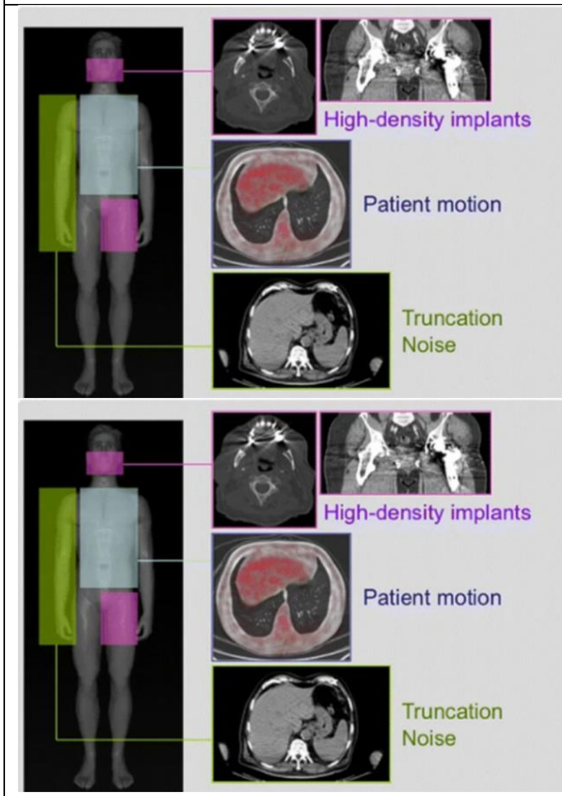
Comment	Image Details
	Image artifact detected and corrected. The most common artifact seen are Hip or knee implants, tooth, respiratory motion that corrected using lung window parameters.

Figure 9: Common artifact sources in PET-CT

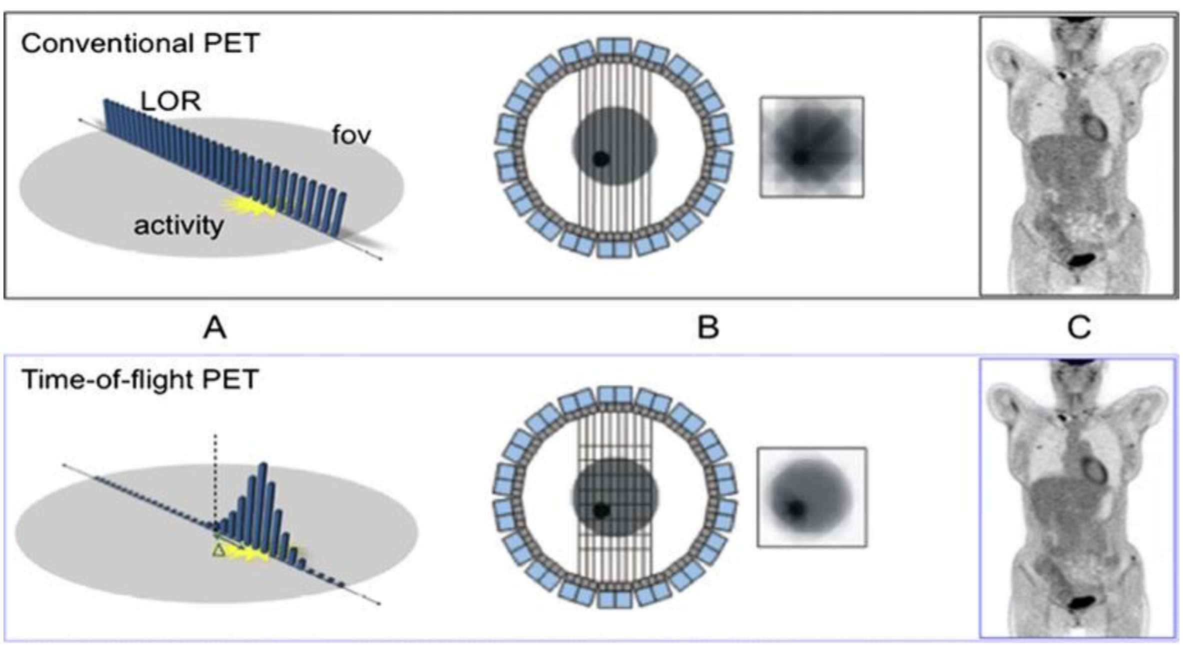


Figure 10: Schematic illustration of the differences between conventional PET (top) and TOF-PET (bottom). Conventional Vs TOF Design.

RESULTS AND DISCUSSION

Breast cancer is the most common cancer in women worldwide. Accurate early diagnosis of breast cancer is critical in the management of the disease. Although mammogram screening has been widely used for breast, cancer screening, high false positive and false-negative rates and radiation from mammography have always been a concern. Over the last 20 years, the emergence of PET that possess a high rate of glucose uptake for breast cancer cells. Such cancer can be successfully imaged with ^{18}F-FDG. PET imaging is the map that representing the positron decay occurred after the radiotracer injection and distribution through human body. The combination of both CT and PET used to provide more accurate quantitative morphological data correction of the quantitative data. The PET row data stored as sinogram mode then mathematically reconstructed into tomographic slices. For butter attenuation correction as well as getting the best image quality the iterative method replaced the filter back projection in the new generation models.

Quantitative analyses in nuclear medicine are increasingly used, both for diagnostic and therapeutic purposes. The Partial Volume Effect (PVE) is the most important factor of loss of quantification in Nuclear Medicine, especially for evaluation in Region of Interest (ROI) smaller than the Full Width at Half Maximum (FWHM) of the PSF. Partial volume effects (PVE) are caused by the limited spatial resolution of the γ camera and the sampling of the reconstructed images into the matrix. PVE depend on the size and shape of the imaged object, the contrast between adjacent objects, the spatial resolution of the camera, and the voxel size. The clinical impact of partial volume effect correction (PVC) significantly affects the SUV and SUVmax respectively in vivo PET imaging using 18F-FDG. Effect of TOF and PVE in the breast. Gaussian filter with 5 mm FWHM is the most common used in the purpose of image smoothing. The source of data and the collection method of this literature were from Google Scholar, PubMed and JNM database about the role of PET/CT in oncology and the effect of quantitative mage analysis parameters in tumor imaging. Table 3 and table 4 summarized the main findings in the literature between 2004 up to 2021.

Table 3: Detailed references in the reviewed studies

Citation	Year	Goal and Purpose	Study Design	Main Findings
[1]	2021	Role of hybrid modalities in imaging	Primary study	Advance hardware image fusion in MI modalities
[2]	2020	The recent advance of PET/CT in clinical RT	Literature review	The strength role of PET in RT patient treatment plan
[3]	2021	Improve image quality and dose constancy	Clinical trials Patient sample	To identify optimal reconstruction parameters
[4]	2015	Updates in TOF	Image parameters and diagnostic review	Significant advantages of TOF and PVE
[5]	2007	Determination of quantitates analysis measurement	Experimental and Clinical trials	Practical impacts of PVEC
[6]	2008	Role of TOF in PET-CT imaging	Experimental and clinical result	Significant improvement of TOF in oncology imaging
[7]	2017	Role of PET in early diagnosis of BC	Primary study	PET as hybrid imaging tool
[8]	2015	Properties of different crystal material used in PET physics	Experimental and literature review	Assessment methods using 3D in-vivo dosimetry
[9]	2017	State of Art in PET	Discussion and primary study	Image quality assessment in PET
[10]	2019	Clinical management of neurological disease in oncology	Primary research study	The effect of patient treatment plan using chemo therapy
[11]	2018	BC management using medical imaging techniques	Research study	The cancer cells in nature
[12]	2018	Effects of BC in women worldwide	Research study	Evolution in female breast cancer imaging
[13]	2004	Determine the tumor homogeneity parameters	Patient sample and Plate form	The development strategies of patient care

Table 4: Detailed references in the reviewed studies

Citation	Year	Goal and Purpose	Study Design	Main Findings
[14]	2011	Evaluation of biological prognosis factors in BC	Patient sample	Triple negative BC and positive progesterone receptors are not affecting SUV uptake
[15]	2004	Reducing acquision time in imaging	Clinical trials	Overview in PET image processing
[16]	2017	Clinical decision in oncology	Literature review	The coast effectiveness of PET and its history
[17]	2012	Application development	Literature review	Fundamental of PET physics
[18]	2010	Challenges in PET system	Literature review	Role of TOF, PVE and PSF in post reconstruction imaging
[19]	2015	Pathological factors of tumor structure imaging	45 patient sample study	The SUVmax tool in the assessment of aggressive BC

				cases
[20]	2014	PET scan count rate	Experiment	Live time PET model, new measurement method
[21]	2007	The relation between MRI DCM and PET-FDG	Retrospective review of medical records	Triple negative tumor affected by SUVmax
[22]	2013	Benefit of PET in evaluation post chemo patient	68 patient sample analysis	Assessment of predictive value parameters in advance BC
[23]	2018	The predict outcomes of residual tumor uptake	Prospective study	Early changes in FDG tumor uptake during neoadjuvant chemotherapy
[24]	2012	PVE as post iterative processing method	Experiment and NEMA	PVE generate an accurate reading uptake compared to voxel data
[25]	2007	Innovation of Hybrid imaging	Literature review	SPECT compared to PET imaging role
[26]	2007	LSYO crystal role in PET physics	NEMA experimental procedure Qc	The best image quality achieved in improving TOF in PET system

CONCLUSION

Fluorodeoxyglucose (^{18}F-FDG) is the earliest radiotracer in positron emission tomography PET body imaging. It accumulates chiefly in the pathological lesion, so the high contrast between lesion and surrounding tissue from the basis for the success of FDG-PET imaging. FDG can detect primary, loco regional and systematic metastases of breast cancer. The greatest clinical role of PET at present in the evaluation of systematic metastatic disease. It is difficult to recommended PET for routine evaluation of the breast or loco regional lymph nodes unless neoadjuvant chemotherapy is planned or internal mammary-suspected metastases.

Image processing in nuclear medicine and PET/CT play significant role in early detection of multi cancerous disease. Furthermore, it is supporting the oncologist treatment plan after the initial diagnose occurred. Based on the literature review journal papers above we can summaries the following:

1. PSF was the most effective algorithm reconstruction correction method in improving the image quality in Breast Cancer cases as well as other types of sensitive cancer cases like brain.
2. Clinically Time of Flight information technique is very useful in improving PET image quality and reducing other image artifact like implant and dental metal artifact.
3. SNR increases overall with post-processing deconvolution techniques.
4. LSO act as the greatest scintillator crystal used in PET/CT according to their outstanding properties like high light output and high stopping power.
5. Quantitative metrics like PVE, TOF, SUV, SUVmax and PSF are the state of art in all PET generation image-processing program.
6. PET has an important and growing role in the management of breast cancer.

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Abbreviations:

The following abbreviations used in this manuscript:

PET/CT	Positron Emission Computed Tomography
TOF	Time of Flight

PVE Partial Volume Effect

PSF Point Spread Function

BGO Bismuth Germinate

LSO Lutetium-oxo orthosilicate crystals

REFERENCES

1. Lalith Kumar Shiyam Sundar a, Otto Muzik b, Ir`ene Buvat c, Luc Bidaut d, Thomas Beyer Potentials and caveats of AI in hybrid imaging. April 2021.
2. Unterrainer, M., Eze, C., Ilhan, H., Marschner, S., Roengvoraphoj, O., Schmidt-Hegemann, N. S., Walter, F., Kunz, W. G., Rosenschöld, P., Jeraj, R., Albert, N. L., Grosu, A. L., Niyazi, M., Bartenstein, P., & Belka, C. (2020). Recent advances of PET imaging in clinical radiation oncology. Radiation oncology, 15(1), 88.
3. Gould, SM., Mackewn, J., Chicklore, S. Optimization of CT protocols in PETCT across different scanner models using different automatic exposure control methods and iterative reconstruction algorithms. EJNMMI Phys 8, 58 (2021).
4. Suleman Surti, Ph.D., Department of Radiology, Perelman School of Medicine, University of Pennsylvania, Philadelphia. Updates on Time-of-Flight PET Imaging Jan 2015.
5. Marine Soret, Stephen L. Bacharach and Irène Buvat Partial-Volume Effect in PET Tumor Imaging Journal of Nuclear Medicine June 2007, 48 (6) 932-945;
6. Karp, J. S., Surti, S., Daube-Witherspoon, M. E., & Muehllehner, G. (2008). Benefit of time-of-flight in PET: experimental and clinical results. Journal of nuclear medicine. Society of Nuclear Medicine, 49(3), 462–470.
7. Aresia Aroztegui AP, García Vicente AM, Alvarez Ruiz S, Delgado Bolton RC, Orcajo Rincon J, Garcia Garzon JR, de Arcocha Torres M, Garcia-Velloso MJ; Oncology Task Force of the Spanish Society of Nuclear Medicine and Molecular Imaging. 18F-FDG PET/CT in breast cancer: Evidence-based recommendations in initial staging. Tumor Biol. Oct 2017.
8. F. Hueso-González, A.K. Biegun, P. Dendooven, W. Enghardt' F. Fiedler, C. Golnik, K. Heidel, T. Kormoll[1], J. Petzoldt[1], K.E. Römer. Comparison of LSO and BGO block detectors for prompt gamma imaging in ion beam therapy 2015 *JINST* 10 P09015.
9. Leesa Ross and Dusty York. European Association of Nuclear Medicine Quality Control of Nuclear Medicine Instrumentation and Protocol Standardization. 2017.

10. April Alcantara, Gholam R. Berenji , Carole S. Scherling , Beata Durcanova , Daniel Diaz-Aguilar,and Daniel H.S. Silverman. Long-Term Clinical and Neuronuclear Imaging Sequelae of Cancer Therapy, Trauma, and Brain Injury 2019.
11. Feng Y, Spezia M, Huang S, Yuan C, Zeng Z, Zhang L, Ji X, Liu W, Huang B, Luo W, Liu B, Lei Y, Du S, Vuppalapati A, Luu HH, Haydon RC, He TC, Ren G. Breast cancer development and progression: Risk factors, cancer stem cells, signaling pathways, genomics, and molecular pathogenesis. 2018 May 12;5(2):77-106.
12. Caleffi, M., Filho, D. D., Borghetti, K., Graudenz, M., Littrup, P. J., Freeman-Gibb, L. A., Zannis, V. J., Schultz, M. J., Kaufman, C. S., Francescatti, D., Smith, J. S., Simmons, R., Bailey, L., Henry, C. A., & Stocks, L. H. (2004). Cryoablation of benign breast tumors: evolution of technique and technology. Breast (Edinburgh, Scotland), 13(5), 397–407.
13. Nioche, C., Orlhac, F., Boughdad, S., Reuzé, S., Goya-Outi, J., Robert, C., Pellot-Barakat, C., Soussan, M., Frouin, F., & Buvat, I. (2018). LIFEx: A Freeware for Radiomic Feature Calculation in Multimodality Imaging to Accelerate Advances in the Characterization of Tumor Heterogeneity. *Cancer research*, *78*(16), 4786–4789.
14. Groheux, D., Giacchetti, S., Moretti, J. L., Porcher, R., Espié, M., Lehmann-Che, J., de Roquancourt, A., Hamy, A. S., Cuvier, C., Vercellino, L., & Hindié, E. (2011). Correlation of high 18F-FDG uptake to clinical, pathological and biological prognostic factors in breast cancer. European journal of nuclear medicine and molecular imaging, 38(3), 426–435.
15. Alessio AM, Kinahan PE, Cheng PM, Vesselle H, Karp JS. PET/CT scanner instrumentation, challenges, and solutions. Radiol Clin N Am. 2004;42(6):1017-32.
16. Ren-Yuan Zhu Quality of Long LSO/LYSO Crystals, 2012.
17. Saif, M. W., Tzannou, I., Makrilia, N., & Syrigos, K. (2010). Role and cost effectiveness of PET/CT in management of patients with cancer. The Yale journal of biology and medicine, 83(2), 53–65.
18. Vaquero, Juan José, and Paul Kinahan. "Positron Emission Tomography: Current Challenges and Opportunities for Technological Advances in Clinical and Preclinical Imaging Systems." Annual review of biomedical engineering vol. 17 (2015): 385-414.
19. Soussan, M., Orlhac, F., Boubaya, M., Zelek, L., Ziol, M., Eder, V., & Buvat, I. (2014). Relationship between tumor heterogeneity measured on FDG-PET/CT and pathological prognostic factors in invasive breast cancer. PloS one, 9(4).
20. Macdonald, L. R., Schmitz, R. E., Alessio, A. M., Harrison, R. L., Lewellen, T. K., & Kinahan, P. E. (2007). Estimating Live-Time for New PET Scanner Configurations. IEEE

Nuclear Science Symposium conference record. Nuclear Science Symposium, 4, 2880–2884.

21. Bolouri, M. S., Elias, S. G., Wisner, D. J., Behr, S. C., Hawkins, R. A., Suzuki, S. A., Banfield, K. S., Joe, B. N., & Hylton, N. M. (2013). Triple-negative and non-triple-negative invasive breast cancer: association between MR and fluorine 18 fluorodeoxyglucose PET imaging. Radiology, 269(2), 354–361.
22. Molina-García, D., García-Vicente, A. M., Pérez-Beteta, J., Amo-Salas, M., Martínez-González, A., Tello-Galán, M. J., Soriano-Castrejón, Á., & Pérez-García, V. M. (2018). Intratumoral heterogeneity in ^{18}F-FDG PET/CT by textural analysis in breast cancer as a predictive and prognostic subrogate. Annals of nuclear medicine, 32(6), 379–388.
23. Groheux D, Hindié E, Giacchetti S, Triple-negative breast cancer: early assessment with 18F-FDG PET/CT during neoadjuvant chemotherapy identifies patients who are unlikely to achieve a pathologic complete response and are at a high risk of early relapse. J Nucl Med 2012;53(2):249–254.
24. Teo BK, Seo Y, Bacharach SL, et al. Partial-volume correction in PET: validation of an iterative post reconstruction method with phantom and patient data. J Nucl Med 2007;48(5):802–810.
25. Beyer, T., Townsend, D.W., Czernin, J. The future of hybrid imaging part 1 and 2 PET/CT. Insights Imaging 2, 225–234 (2011).
26. Surti S et al (2007) Performance of Philips Gemini TF PET/CT scanner with special consideration for its time-of-flight imaging capabilities. J Nucl Med 48(3):471–480