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RESEARCH ARTICLE

THE EFFECTIVE VALUE OF PET/CT IN DIAGNOSING CARDIOVASCULAR DISEASE AND PEDIATRIC CANCER; A COMPARATIVE STUDY

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Abstract

Overview: Combined PET/CT systems have emerged as promising imaging modalities and are being more routinely used in clinical situations. ¹⁸F-FDG PET/CT is an established entity in the work-up of several oncologic disorders and is making forays in the diagnosis of inflammatory diseases, leading to increased use for cardiac and neurologic applications. Although PET is on the move in cardiovascular medicine and new developments are likely to increase its application and impact in clinical practice, some similarities and interrelationships between its cardiac applications and applications for tumor imaging should be noted.

The study aimed to prospectively study the clinical experience with PET/CT in Cardiac diseases and in pediatric malignancies to evaluate and compare the efficacy of this imaging system in both diseases, and to determine if it provided additional diagnostic information on the disease status.

Methodology: Thirty two cardiac patients with previous history of myocardial infarction & left ventricular dysfunction and coronary artery disease (CAD) were underwent the imaging procedures consisting of PET/CT, echocardiography and invasive angiography. Diagnostic sensitivity of these less invasive modalities for detection of myocardial viability was compared to invasive coronary angiography. Additionally, 54 pediatric cancer patients were included in this study [28 had Lymphoma and 26 had soft tissue sarcoma (STS)]. Seventy two scans were performed for whole body in all patients for initial diagnosis and staging.

Results: In the current study, Coronary angiography was used as the gold standard; PET/CT has high diagnostic value in the assessment of myocardial viability when compared to echocardiography; and also in malignant disease if distant metastases or second primary tumors are detected with regard to staging of the primary tumor. It may influence the treatment decision in both diseases. The diagnostic sensitivity of cardiac PET/CT, cardiac angiography and echocardiography was 98.2%, 93.4% and 82.5%, respectively. Diagnostic sensitivity of PET/CT in myocardial viability at per-vessel based assessment

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was 80.2% for LAD (left anterior descending), 77.6% for LCX (left circumflex), and 100% for RCA (right coronary) coronary arteries. The overall sensitivities, specificities & positive and negative predictive values of the imaging system for all the suspicious sites in pediatric malignancy were 94.22%, 92.72%, 93.68% and 93.33% respectively. The sensitivities and specificities for initial staging of malignant lymphomas were ranged 70%-100% and 90.48%-100% respectively. They ranged 80%-100% and 92%-100% respectively in STS.

Conclusion: The study concluded that the PET/CT is the gold standard for noninvasive functional imaging in cardiovascular disease as well as in oncology. It has high diagnostic value in the assessment of myocardial viability in patients with known CAD. Technical developments in PET/CT scanning in cancer management may increase the precision of radiotherapy planning and thus improve tumor control and reduce treatment-related morbidity. The use of PET/CT in the management of pediatric malignancy is recommended to facilitate the sparing of normal structures and the escalation of dose. Further studies are recommended in cardiovascular patients for the incorporation of PET/CT into patient management is warranted.

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Introduction:-

Cardiovascular diseases are progressive and there are a number of physiological and morphological changes that occur with aging that could alter cardiovascular function and subsequently increase risk of cardiovascular disease (Li et al., 2014). Despite considerable advances in prevention and treatment over the last decades, cardiovascular diseases remain the most frequent causes of death worldwide and represent a great challenge for modern research and medicine. This requires urgent development of sensitive and noninvasive methods for early detection and personalized treatment of cardiovascular diseases (Gaemperli and Kaufmann, 2011). Traditional medical imaging techniques have been routinely used to provide early diagnosis and prognosis of cardiovascular diseases (Schwaiger et al., 2010). Ideally it would be possible to detect molecular and cellular processes early and characterize cardiovascular diseases before manifestation of gross anatomical features or physiological consequences. Current advanced molecular imaging modalities include positron emission tomography (PET), single photon emission computed tomography (SPECT), magnetic resonance imaging (MRI), and optical imaging, all of which could provide critical molecular and cellular level information for early diagnostics, advanced therapeutics, and better understanding of fundamental biological processes of cardiovascular disease (Jang et al., 2012; Li et al., 2014).

Positron emission tomography (PET) has contributed significantly to the advances in our understanding of cardiac physiology and pathophysiology for more than 20 years (Nekolla et al., 2009). The introduction of PET/CT scanners combined the functional data of PET with the detailed anatomic information of CT into a single examination. The poor spatial resolution of PET is substantially compensated for by integrated PET/CT, with co-registration of functional imaging with PET and anatomic imaging with CT (Xu et al., 2012/2015). In addition to being a powerful research tool in cardiology, recent technical development and improved availability facilitated also its routine clinical use in cardiology. PET is the most reliable non-invasive tool for the identification of myocardial viability and also allows accurate assessment of myocardial perfusion and coronary artery disease (CAD), which is known to be the leading cause of mortality in adults. Assessment of myocardial perfusion plays an important role in the diagnostic work-up of patients with suspected CAD as well as in the assessment of prognosis and guiding of therapy in patients with established CAD (Nekolla et al., 2009).

Although PET is on the move in cardiovascular medicine and new developments are likely to increase its application and impact in clinical practice, some similarities and interrelationships between its cardiac applications and applications for tumor imaging should be noted. First, the success of PET as a key modality in tumor staging and evaluation of anti-tumor therapy has resulted in dissemination of the technique and in improved availability for cardiac imaging. Second, expensive equipment, such as scanners, radiochemistry laboratories, and cyclotrons, is most effectively used when it serves multiple areas of PET imaging applications. And finally, many existing and novel biologic targets for PET imaging are important not only in heart and vessels, but also in tumors. This is highly

relevant not only because advances in tumor biology may help advance cardiovascular biology via improved understanding of related biomechanisms, but also because multiple applications in heart, vessels, and tumors will be helpful to stimulate interest in commercialization of compounds with a broader spectrum of target groups (Bengel et al., 2009).

Cardiac PET imaging is another well-established tool for the evaluation of ischemia, blood flow quantification, myocardial viability and perfusion (Berman et al., 2006; Machac, 2005). Cardiac PET utilizing ^{18}F -FDG is considered the most sensitive modality for detecting hibernating viable myocardium and predicting left ventricular functional recovery post-coronary revascularization. PET has higher spatial and temporal resolution than SPECT due to more robust methods of attenuation correction, thus, PET allows quantification of resting and hyperemic regional myocardial perfusion. When PET was integrated into clinical patient management, a significant reduction in cardiac events was observed in patients with ^{18}F -FDG PET-assisted management, according to randomized controlled trials (Abraham et al., 2010; Beanlandset al., 2007). PET images provide incremental prognostic information to the clinical and angiographic findings with regard to event-free survival. An increased extent and severity of perfusion defects with stress PET were reported to be associated with increased frequency of adverse cardiac events, thus, this indicates PET can be used to predict cardiac mortality (Dorbala et al., 2009). Cardiac PET is not yet as widely available as SPECT imaging. Furthermore, experience in image interpretation and operation may vary widely. Cardiac PET will continue to play a key role in the investigation of myocardial viability and perfusion contributing more to available data (Sun, 2013).

Combined PET and CT systems (PET/CT) have emerged as promising imaging modalities and are being more routinely used in clinical situations (von Schulthess et al., 2006). Although many studies about whole-body PET/CT for various cancers were done, the results were still controversial and inconclusive. In several previous studies, ^{18}F -FDG PET/CT was shown to be more sensitive and specific than conventional imaging procedures for the detection of distant malignancies in cancer patients at initial staging before treatment or restaging after treatment (Antoch et al., 2004; Fuster et al., 2008; Ng et al., 2009; Strobel et al., 2007; Veit-Haibach et al., 2009). Despite growing numbers of reports on imaging adult malignancies with PET/CT, little data have been reported so far about the clinical relevance of this modality in pediatric patients (Xu et al., 2012/2015).

Although radiation exposure from CT when used for attenuation correction can be limited (Souvatzoglou et al., 2007), the radiation dose from coronary CT angiography (CTA) is >10 mSv in recent clinical trials has been >10 mSv, which is clearly higher than from standard radiography or X-ray angiography (Bluemke et al., 2008). Moreover, precise alignment between emission and “transmission” PET images may benefit from repeated, simultaneously acquired attenuation maps. – From a practical point of view, advances in CT technology are likely to result in substantial changes in hardware in hybrid PET/CT systems while advances in MRI are frequently based on imaging sequences and less complex pieces of hardware, such as coils, which makes upgrading easier and less expensive. – Both cardiac MRI and PET examinations can be rather time consuming. Thus, improvements in patient compliance as a result of reduced scan time could be significant, particularly in patients with dyspnea due to heart failure who have difficulty holding their breath during MRI acquisitions (Nekollaet al., 2009).

The study aimed to prospectively study the clinical experience with ^{18}F -FDG PET/CT in Cardiac disease and in pediatric malignancies to evaluate and compare the efficacy of this new imaging system in both disease, and to determine if PET/CT provided additional diagnostic information on disease status.

Patients and Methods:-

Cardiac patients:-

A multi-centric prospective study that involved patients with previous history of myocardial infarction & left ventricular dysfunction and coronary artery disease (CAD) over a period of 6 months was performed. All patients were suggested to undergo full clinical history and examination, cardiac PET/CT myocardial viability, echocardiography and invasive coronary angiography examinations with an interval of less than 20 days between the imaging tests. Coronary angiography was used as the gold standard. Thirty two patients (17(53.1%) male & 15(46.9%) female; mean age 58.5 ± 10.5 years) are concluded in the study. Consent forms were obtained from all patients, and ethical approval was granted from institutional review boards.

All patients were informed for fasting at least 6 h before the scan and baseline blood sugar was checked. Blood sugar was checked 45–60 min after injection of a glucose loading dose (50–75 g). If it was < 140 mg/dL, a 444

MBq(12 mCi) of ^{18}F -FDG was injected intravenously. If it was > 140 mg/dL, intravenous regular insulin was injected according to blood glucose level. Myocardial ^{18}F -FDG PET/CT study was performed 45–60 min after injection of ^{18}F -FDG. The data were analyzed based on a 5-point scale examining the segment of three main coronary arteries, namely: left anterior descending (LAD), left circumflex (LCX) and right coronary artery (RCA): 0 = normal perfusion, 1 = mild defect, 2 = moderate defect, 3 = severe defect and 4 = absent uptake. For echocardiography, the assessment used was according to the 16-segment model as recommended by the American Society of Echocardiography (Klocke et al., 2003).

Coronary angiography was carried out using the standard Seldinger's technique on an angiographic machine by femoral approach which was performed by cardiologists. The minimal lumen diameter was measured in projections showing the most severe narrowing. The degree of stenosis was classified into four categories: (1) no stenosis, (2) minimal or mild stenosis ($\leq 50\%$), (3) moderate stenosis (50% – 70%), and (4) severe stenosis ($> 70\%$). CAD was defined when lumen diameter reduction was greater than 50% (moderate or severe stenosis).

Resting echocardiography was performed by a consultant cardiologist using a standard protocol. Images were acquired in the normal parasternal long-axis and short-axis views, with particular attention paid to determine the regional cardiac function. Calculations of the regional wall motion were assumed using a 16-segment model according to the American Society of Echocardiography (American Society of Nuclear Cardiology Imaging guidelines., 1999; Cerqueria et al., 2002; Schiller et al., 1989). These 16 segments were classified as 0 = normal; 1 = hypokinetic; 2 = akinetic; and 3 = dyskinetic. The segments founded within the infarction-related coronary segment were the segments analyzed for wall motion. Then, the regional wall motion score was calculated.

Pediatric Patients with Malignancy:-

Fifty four pediatric patients (33(61.1%) male and 21(38.9%) female) with suspected or known malignancy, evaluated by ^{18}F -FDG imaging using a combined PET/CT system, between May 2011 and October 2015, included in the study. The male to female ratio was 1.57:1. The patient's age was from 9 month to 18 years (y) old with a median age of 12 y at their first PET/CT examination. 33 (66.7%) of the patients were below 10 years old. Twenty eight patients had lymphoma and 26 had STS soft tissue sarcoma. The indication, purpose, and findings of each PET/CT examination were taken in consideration, in addition to other imaging findings as well as clinical information. PET/CT examination was performed for whole body in all patients (72 scan) for initial diagnosis and staging.

Three hundred and twenty four suspicious sites were evaluated in the 54 included patients. Patients were selected according to their reports which indicate areas of increased FDG uptake. PET findings were considered positive when uptake occurred at sites of suspected disease, in asymmetrical lymph nodes or in nodes unlikely to be affected by inflammation (mediastinal, except for hilar, and abdominal). PET findings were adjudged negative for neoplastic localizations in the following instances: physiological uptake (urinary, muscular, thymic or gastrointestinal), symmetrical nodal uptake, very low uptake and non-focal uptake. PET findings were compared with the results of other diagnostic procedures (including CT and ultrasound), biopsy findings and other clinical data.

After at least 4 h of fasting, a total body PET scan was done one hour after IV injection of 300 MBq of ^{18}F -FDG. 64 MSCT scan was performed using GE Discovery VCT simultaneously and used for attenuation correction, anatomical localization and diagnosis. Max. Variant of SUV; a semi-quantitative analysis would be done for selected ROI.s and the normal threshold is <2.5 .

Statistical Analysis:-

The usefulness of diagnostic tests is known as their ability to detect a person with disease or exclude a person without disease. It is usually described by terms such as sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) (Akobeng, 2007).

- **Sensitivity** is the ability of a test to correctly classify an individual as 'diseased', i.e. probability that a test result will be positive when the disease is present (true positive rate) (Parikh et al., 2008). *Sensitivity* = the number of ill persons with positive test results / the number of all persons who have the disease (Nyari, 2011).
- **Specificity** is the ability of a test to correctly classify an individual as disease-free is called the test's specificity, i.e. the probability that a test result will be negative when the disease is not present (true negative rate) (Parikh et al., 2008). *Specificity* = the number of healthy persons with negative test results / the number of all healthy persons (Nyari, 2011).

- **Positive Predictive Value (PPV)** is the probability that the disease is present when the test is positive (MedCalc Software., 2016). $PPV = \frac{\text{the number of persons diagnosed as have that disease with positive test results}}{\text{the number of all positive test results}}$ (Nyari, 2011).
- **Negative Predictive Value (NPV)** is the probability that the disease is not present when the test is negative (MedCalc Software, 2016). $NPV = \frac{\text{the number of healthy persons with negative test results}}{\text{the number of all negative test results}}$ (Nyari, 2011).
- **Prevalence** is defined as the prior probability of the disease before the test is carried out (Peacock and Peacock, 2011). *Prevalence* rate is the total number of cases of a disease existing in a population divided by the total population (Health.ny.gov, 2015).
- **Accuracy** is the efficiency of a test that indicates the percentage of patients who are correctly classified as having disease or not having disease (Mahon et al., 2011). $Accuracy = \frac{\text{the total number of ill persons with positive test results and healthy persons with negative test results}}{\text{the total number of population}}$.

Results:-

Cardiac Patients:-

The patient's characteristics are shown in table (1). A total of 1088 segments in all patients were analyzed for cardiac PET/CT imaging examinations, while for echocardiography there were 512 segments that were analyzed in comparison with PET findings. Comparison was also performed between the accuracy of coronary PET and that for angiography and echocardiography. All patients were found to have CAD and the triple vessel disease with $\geq 50\%$ stenosis involving LAD, LCX and RCA was found in 37.5% of them, and revealing severely reduced FGD uptake in different regions. By invasive coronary angiography, there were a significant coronary stenosis or occlusion ($> 70\%$ lumen stenosis); with mild to moderate stenosis in 260 of the coronary arteries (LAD, LCX, and RCA) and by echocardiography it was found in 230 of the coronary arteries. So, the cardiac PET has the highest diagnostic value in the assessment of all of the three main coronary arteries.

Table 1:-patients Characteristics:

Items	Patients		Items	Patients	
	No.	%		No.	%
<i>Diagnoses:</i>			<i>Risk factors:</i>		
Ischemic Heart Disease	4	12.5	Hypertension	26	81.3
Ischemic Dilated Cardiomyopathy	7	21.9	Diabetes Mellitus	24	75
Thrombolysis	6	18.8	History of Smoking	5	15.6
Myocardial Infarction	3	9.4	Dyslipidemia	10	31.3
Triple Vessel Disease	12	37.5	Obesity	13	40.6
Double Vessel Disease	10	31.3			

The diagnostic sensitivity of cardiac PET/CT, cardiac angiography and echocardiography was 98.2%, 93.4% and 82.5%, respectively, as shown in Figure (1). The specificity was not analyzed, since all patients had confirmed CAD, (true negative value was zero).

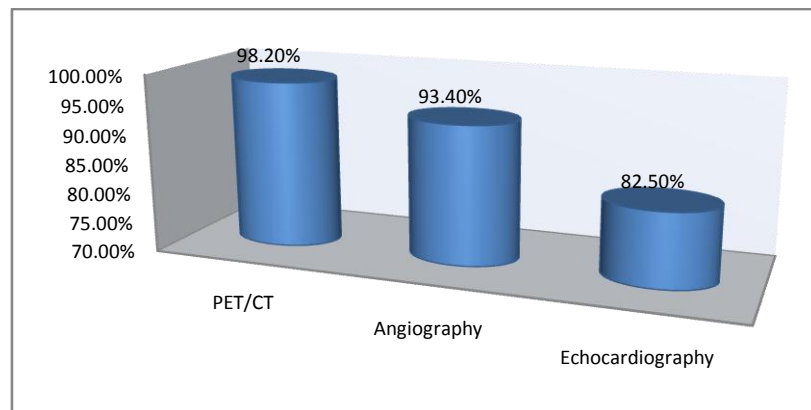


Figure 1:-Diagnostic sensitivity of cardiac PET/CT, cardiac angiography and echocardiography

Diagnostic sensitivity of PET/CT in myocardial viability at per-vessel based assessment was 80.2% for LAD, 77.6% for LCX, and 100% for RCA coronary arteries (figure 2)

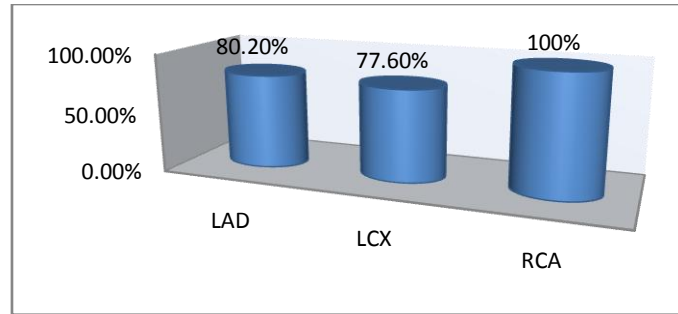


Figure 2:- Diagnostic sensitivity of PET/CT in myocardial viability at per-vessel based assessment

The mean score for assessment of myocardial viability by PET/CT at per-vessel based analysis was 3.5 ± 0.83 , 3.9 ± 0.44 , and 4.1 ± 0.10 , corresponding to the LAD, LCX and RCA coronary arteries, respectively (table 2). The cardiac PET/CT was found to be superior in terms of image quality with more accurate assessment of all of the segments.

Table 2:- The mean score for assessment of myocardial viability by PET/CT at per-vessel based analysis

Item	LAD	LCX	RCA
The mean score	3.5 ± 0.83	3.9 ± 0.44	4.1 ± 0.10

Pediatric Patient with Malignancy:-

The results of the present work are presented in tables (3-6). A table (3) shows the patients characters. The stage of the malignant disease patients can be seen before and after the evaluation by PET/CT in table (4).

Table 3:-Patients Characteristics

Items	Lymphoma (28 Patients)		Soft Tissue Sarcoma (26 patients)		Total (54 patients)	
	No.	%	No.	%	No.	%
Age						
<10years	21	75	15	57.7	36	66.7
>10 years	7	25	11	42.3	18	33.3
Sex						
Male	16	57.1	17	65.4	33	61.1
Female	12	42.9	9	34.6	21	38.9
Stage						
I	9	32.1	6	23.1	15	27.8
II	7	25	3	11.5	10	18.5
III	8	28.6	16	61.5	24	44.4
IV	4	14.3	1	3.9	5	9.3
Tumor size						
>5cm	18	64.3	18	69.2	36	66.7
<5cm	10	35.7	8	30.8	18	33.3
Metastases:						
Present	8	28.6	2	7.7	10	18.5
Absent	20	71.4	24	92.3	44	81.5

Table 4:-Evaluating the Stage of Pediatric Malignancy by of PET/CT Scan

Stage	Lymphoma (28 Patients)		Soft Tissue Sarcoma (26 patients)		Total (54 patients)	
	Before PET/CT	After PET/CT	Before PET/CT	After PET/CT	Before PET/CT	After PET/CT
I	9	7	4	5	13	12
II	7	10	5	4	12	14
III	8	9	14	16	22	25
IV	4	2	3	1	7	3

The true positive and negative sites of the 324 regions analyzed, was 163 and 140 respectively. The overall sensitivities, specificities & positive and negative predictive values of the imaging system for all the suspicious sites were 94.22%, 92.72%, 93.68% and 93.33% respectively. (Tables 5)

The sensitivities and specificities of 18F-FDG PET/CT for initial staging of malignant lymphomas were ranged 70%-100% and 90.48%-100% respectively. They ranged 80%-100% and 92%-100% respectively in STS. The negative and positive predictive values in evaluating the stage of lymphoma were 85.71%-100% and 50%-100% respectively. It was 83.33% -100% and 33.33% -100% respectively for STS (Table 6).

Table 5:- Efficacy of PET/CT Scan in Detecting the Site of Lesion in Pediatric Malignancy

PET/CT Scan	Prevalence	Sensitivity	Specificity	PPV	NPV	Accuracy
Head & Neck	60.34%	94.30%	86.96%	91.67%	90.91%	91.38%
Chest	37.25%	84.21%	96.88%	94.12%	91.18%	92.16%
Abdomen & Pelvis	58.47%	98.55%	95.92%	97.14%	97.92%	97.46%
Extremities	40.63%	92.31%	94.74%	92.31%	94.74%	93.75%
Bony skeleton	40.91%	88.89%	84.62%	80.00%	91.67%	86.36%
Body LN chains	65.12%	92.86%	86.67%	92.86%	86.67%	90.70%
Total	53.40%	94.22%	92.72%	93.68%	93.33%	93.52%

PPV: Positive predictive value, NPV: Negative predictive value

Table 6:- Efficiency of PET/CT Scan in Evaluating the Stage of Pediatric Malignancy

PET/CT Scan	Prevalence	Sensitivity	Specificity	PPV	NPV	Accuracy
Lymphoma						
Stage I	25.00%	100.00%	90.48%	77.78%	100.00%	92.86%
Stage II	35.71%	70.00%	100.00%	100.00%	85.71%	89.29%
Stage III	32.14%	88.89%	100.00%	100.00%	95.00%	96.43%
Stage IV	7.14%	100.00%	92.31%	50.00%	100.00%	92.86%
Soft Tissue Sarcoma						
Stage I	19.23%	80.00%	100.00%	100.00%	95.45%	96.15%
Stage II	15.38%	100.00%	95.45%	80.00%	100.00%	96.15%
Stage III	61.54%	87.50%	100.00%	100.00%	83.33%	92.31%
Stage IV	3.85%	100.00%	92.00%	33.33%	100.00%	92.31%

PPV: Positive predictive value, NPV: Negative predictive value

Discussion:-

Coronary artery disease (CAD) is the leading cause of death in advanced countries and its prevalence is increasing among developing countries (Lloyd-Jones et al., 2010; Gaziano et al., 2010). Various less-invasive imaging modalities are increasingly used in the diagnosis of CAD including coronary CT angiography, cardiac magnetic resonance imaging (MRI), and cardiac single photon emission computed tomography (SPECT), positron emission tomography (PET) and integrated SPECT/CT and PET/CT (Sun et al., 2011). To improve early diagnosis and patient management, it is essential to have an overview of the diagnostic value of different imaging modalities in CAD (Sun, 2013). Due to their success in oncology, all currently offered PET imaging systems are hybrid PET-CT scanners. This has brought challenges for cardiac imaging that is related mainly to the use of a separate CT for

attenuation correction of subsequently acquired PET data (Bengel et al., 2009). Although less routine than whole-body imaging, cardiac PET using ^{18}F -FDG have been demonstrated as a valuable tool in the adult population and to a lesser degree in children. Cardiac imaging using ^{18}F -FDG plays an important role in the assessment of myocardial viability and can be particularly valuable when used in conjunction with other imaging modalities such as $^{99\text{m}}\text{Tc}$ -sestamibi scanning. To enhance ^{18}F -FDG uptake into viable myocardium, patients are administered oral or intravenous glucose before the injection of ^{18}F -FDG (McQuattie, 2008).

This prospective study investigates the diagnostic value of non-invasive cardiac modalities with the aim of determining myocardial viability in patients with known CAD through comparing ^{18}F -FDG PET/CT and echocardiography with invasive coronary angiography as the gold standard. Our results showed that cardiac ^{18}F -FDG PET/CT has superior diagnostic value in patients with CAD, when compared to echocardiography and cardiac angiography either at per-patient or per-vessel based analysis. The diagnostic sensitivity of cardiac PET/CT, cardiac angiography and echocardiography was 98.2%, 93.4% and 82.5%, respectively. Diagnostic sensitivity of PET in myocardial viability at per-vessel based assessment was 80.2% for LAD, 77.6% for LCX, and 100% for RCA coronary arteries. Although based on a small number of patients, results of this study highlight the high diagnostic value of ^{18}F -FDG PET/CT in the detection of myocardial viability. Combined SPECT/CT and PET/CT systems are today well established in clinical routine imaging with promising results reported (Namdar et al., 2005; Rispler et al., 2007; Groves et al., 2009; Sato et al., 2010; Al Moudi et al., 2011), although more multicentric trials are needed to validate the diagnostic value of the hybrid imaging modalities (Sun, 2013).

Recent advances in radiopharmaceuticals, hardware, and software of cardiac PET imaging have improved the diagnostic accuracy and risk assessment of patients with suspected cardiac disorders (Underwood et al., 2014; Danad et al., 2013; Flotats et al., 2011; Ratib and Nodulous, 2014). For example, the rapid evolution of hybrid PET/CT and PET/MR imaging with the advanced tracers has provided a new perspective on cardiac imaging by providing combined anatomic and functional evaluation of coronary disease and alterations in cardiac function. Because of the pivotal role of tracers in the realization of the power of cardiac PET imaging, the design and development of tracers is becoming one of the major subjects of cardiac PET imaging (Sogbein et al., 2014; Li, 2014). Additionally, the assessment of myocardial viability with ^{18}F -FDG PET is based on its ability to distinguish the two main pathogenic mechanisms for chronic myocardial dysfunction in ischemic cardiomyopathy: irreversible loss of myocardium due to prior myocardial infarction (scar), and at least partially reversible loss of contractility owing to chronic or repetitive ischemia (hibernating myocardium) (Schinkel et al., 2007). The distinctive feature of these two mechanisms is that revascularization has the potential to restore contractile function of the hibernating myocardium but not scar (Ghosh et al., 2010). This distinction may be of paramount importance in clinical decision-making because of the upfront morbidity and mortality associated with revascularization procedures in patients with severe left ventricular dysfunction (Al Moudi et al., 2014). It is likely; however, that increasing availability of 64-slice CT in PET-CT systems, along with new prospectively gated CT acquisition techniques, which lower radiation exposure for CT angiography by more than 70%, will contribute to a more widespread use in hybrid PET-CT protocols. Innovative integrated imaging protocols may include CT for morphologic assessment of coronary arteries and PET for functional assessment of myocardial blood flow. A CT delayed enhancement study may be done after CT angiography to identify the presence or absence of scar. This may obviate the need for a rest perfusion study (Bengel et al., 2009). It should be noted, however, that positron emitting tracers typically provide less radiation burden to the patient when compared with SPECT tracers used for the same diagnostic purpose, which is, in part, due to their much shorter half-lives. Also, the radiation burden to staff involved in cardiac PET imaging has been investigated, and due to differences in radiotracer administration, scan acquisition, and stress-testing tasks, doses with PET seem to be lower for staff (as for patients) when compared with single-photon emitting tracers (Bengel et al., 2009).

Additionally, hybrid tomographs make it possible to perform a rapid and comprehensive evaluation of functional and anatomical severity of CAD by assessment of myocardial perfusion and non-invasive angiography. On the one hand, optimal evaluation of hemodynamic consequences requires integration of anatomical information with demonstration of myocardial ischemia. On the other hand, myocardial infarction and sudden cardiac death result from the rupture of plaques that do not necessitate significant flow limitations. Several features, such as severe luminal obstruction, thin fibrous cap, large lipid core, and the presence of active inflammation are characteristic of vulnerable plaques. Non-invasive imaging of plaque burden in combination with the features of plaque vulnerability might, therefore, lead to an improved assessment of individuals at risk of acute coronary events and help to refine estimates of the cardiovascular risk in the subclinical phase of atherosclerosis (Nekolla et al., 2009). The incremental value of hybrid

imaging lies in accurate spatial co-localization of myocardial perfusion defects and anatomic coronary arteries. This combined technology allows detection and quantification of the burden of calcified and non-calcified plaques, quantification of vascular activity and endothelial health, identification of flow-limiting coronary stenosis, and potentially identification of high-risk plaques in the coronary artery tree (Di Carli and Murthy, 2011).

Successful management of solid tumors in children requires imaging tests for accurate disease detection, characterization, and treatment monitoring. Technologic developments aim toward the creation of integrated imaging approaches that provide a comprehensive diagnosis with a single visit. These integrated diagnostic tests are not only convenient for young patients but also save direct and indirect health-care costs by streamlining procedures, minimizing hospitalizations, and minimizing school or work time lost for children and their parents (Uslu et al., 2015). However, modern radiotherapy techniques heavily rely on high-quality medical imaging. PET provides biologic information about the tumor, complementary to anatomic imaging. Integrated PET/CT has found its way into the practice of radiation oncology, and ^{18}F -FDG PET is being introduced for radiotherapy planning. The functional information possibly augments accurate delineation and treatment of the tumor and its extensions while reducing the dose to surrounding healthy tissues. In addition to ^{18}F -FDG, other PET tracers are available for imaging specific biologic tumor characteristics determining radiation resistance (Troost et al., 2015). The use of ^{18}F -FDG in PET/CT is well documented as a valuable tool in the staging and diagnosis of disease for many oncology patients. Although considered routine in adults, PET/CT in children has been somewhat limited. On the other hand, paramount to any successful PET/CT examination is the establishment of acquisition protocols that allow high quality images to be obtained while ALARA principles are followed (McQuattie, 2008).

In the current study, The overall sensitivities, specificities & positive and negative predictive values of the imaging system for all the suspicious sites were 94.22%, 92.72%, 93.68% and 93.33% respectively. The sensitivities and specificities of ^{18}F -FDG PET/CT for initial staging of malignant lymphomas were ranged 70%-100% and 90.48%-100% respectively. They ranged 80%-100% and 92%-100% respectively in STS. The negative and positive predictive values in evaluating the stage of lymphoma were 85.71%-100% and 50%-100% respectively. It was 83.33% -100% and 33.33% -100% respectively for STS. Some studies reported the sensitivities and specificities of ^{18}F -FDG PET/CT for initial staging of malignant lymphomas were 96%–99% and 95%–100%, respectively (Kabickova et al., 2006; Furth et al., 2006; Cheng et al., 2013; Miller et al., 2006; Paulino et al., 2012; Punwani et al., 2010; Uslu et al., 2015). Others, reported high negative predictive value (negative predictive value, 85.7%–100%; positive predictive value, 41.2%–85.7%) which is comparable to the present study (Riad et al., 2010; Bakhshi et al., 2012; Ilivitzki et al., 2013; Uslu et al., 2015). Furth et al., 2009 reported that a negative ^{18}F -FDG PET/CT scan after 2 cycles of chemotherapy is a strong indicator of relapse-free survival, with a negative predictive value of 100% in HL patients. Therefore, an ^{18}F -FDG PET/CT scan has been advocated by many investigators and has led to early intensification of chemotherapy in apparent non-responders (Furth et al., 2009; Levine et al., 2006; Meany et al., 2007; Uslu et al., 2015). Additionally, PET or PET/CT has clear advantage in evaluating soft-tissue masses and, thus, has been reported to be useful in patients with lymphoma or other malignancies after treatment (Weber, 2005). Early detection of distant malignancies in cancer patients is crucial for guiding subsequent staging procedures and treatment (Xu et al., 2012/2015). In several previous studies, ^{18}F -FDG PET/CT was shown to be more sensitive and specific than conventional imaging procedures for the detection of distant malignancies in cancer patients at initial staging before treatment or restaging after treatment (Ng et al., 2009; Fuster et al., 2008; Antoch et al., 2004; Strobel et al., 2007; Veit-Haibach et al., 2009). The introduction of PET/CT scanners combined the functional data of PET with the detailed anatomic information of CT into a single examination (Xu et al., 2012/2015). The combination of high-quality PET scans with diagnostic or low-dose CT scans aids physicians in the staging, therapy planning, and treatment of many pediatric oncology patients. Fusion of the physiologic PET scan with the anatomic CT scan can help in distinguishing disease from other physiologic processes and can be an invaluable tool for referring physicians when they are evaluating for recurrence of disease. This relatively noninvasive scan can provide, through a single study, information and insight that in previous years required multiple scans using several different imaging modalities (McQuattie, 2008).

Summary and Conclusion:-

Cardiac PET is a powerful, quantitative, noninvasive imaging technique that is increasingly penetrating the clinical arena. For clinical assessment of myocardial perfusion and viability, evidence for diagnostic and prognostic usefulness is increasing and cost-effectiveness due to high accuracy despite high single-test costs is suggested. The advent of hybrid imaging enables routine combination of PET with CT-derived morphologic parameters. New molecular imaging compounds will be key elements in the emerging paradigm of personalized medicine (Bengel et

al., 2009). Additionally, integrated PET/CT has found its way into the practice of radiation oncology, and ^{18}F -FDG PET is being introduced for radiotherapy planning. The functional information possibly augments accurate delineation and treatment of the tumor and its extensions while reducing the dose to surrounding healthy tissues. In addition to ^{18}F -FDG, other PET tracers are available for imaging specific biologic tumor characteristics determining radiation resistance (Troost et al., 2015). The study aimed to prospectively study the clinical experience with ^{18}F -FDG PET/CT in cardiac diseases and in pediatric malignancies to evaluate and compare the efficacy of this new imaging system in both diseases, and to determine if PET/CT provided additional diagnostic information on disease status. The study concluded that the PET/CT is the gold standard for noninvasive functional imaging in cardiovascular disease as well as in oncology. It has high diagnostic value in the assessment of myocardial viability in patients with known CAD. Technical developments in PET scanning in cancer management may increase the precision of radiotherapy planning and thus improve tumor control and reduce treatment-related morbidity. **Recommendation** regarding the use of PET/CT in the management of pediatric malignancy to facilitates the sparing of normal structures and the escalation of dose. Further studies were recommended in cardiovascular patients for the incorporation of PET/CT into patient management is warranted. The goals of future investigation will be to refine these technologies, address the issue of cost-effectiveness, and validate a range of clinical applications in large-scale clinical trials.

Reference:-

1. Abraham, A., Nichol, G., Williams, K.A., Guo, A., deKemp, R.A., Garrard, L., Davies, R.A., Duchesne, L., Haddad, H., Chow, B., DaSilva, J., Beanlands, R.S. and ;PARR 2 Investigators.(2010): ^{18}F -FDG PET imaging of myocardial viability in an experienced center with access to ^{18}F -FDG and integration with clinical management teams: the Ottawa-FIVE substudy of the PARR 2 trial. *J Nucl. Med.*, 51:567-574.
2. Al Moudi, M. and Sun, Z.(2014):Diagnostic value of ^{18}F -FDG PET in the assessment of myocardial viability in coronary artery disease: A comparative study with $^{99\text{m}}\text{Tc}$ SPECT and echocardiography. *J Geriatr. Cardiol.*, 11(3):229–236. doi: 10.11909/j.issn.1671 5411.2014.03.008 PMID: PMC4178515
3. Al Moudi, M., Sun, Z., and Lenzo, N.(2011):Diagnostic value of SPECT, PET and PET/CT in the diagnosis of coronary artery disease: A systematic review. *Biomed Imaging Interv J.*, 7(2): e9.
4. Akobeng, A.K.(2006):Review Article, Understanding diagnostic tests 1: sensitivity, specificity and predictive values. *Journal Compilation, 2007, Foundation ActaPædiatrica. ActaPædiatrica*, 96:338–341.
5. American Society of Nuclear Cardiology Imaging guidelines for nuclear cardiology procedures (1999): Part 2. *J Nucl. Cardiol.*, 6(2):G47–G84.
6. Antoch, G., Saoudi, N., Kuehl, H., Dahmen, G., Mueller, S.P., Beyer, T., Bockisch, A., Debatin, J.F., and Freudenberg, L.S.(2004):Accuracy of Whole-body dual-modality fluorine-18-2-fluoro-2-deoxy-d-glucose positron emission tomography and computed tomography (FDG-PET-CT) for tumor staging in solid tumor: comparison with CT and PET. *J Clin. Oncol.* 22(1):4357–4368.
7. Bakhshi, S., Radhakrishnan, V., Sharma, P., Kumar, R., Thulkar, S., Vishnubhatla, S., Dhawan, D., and Malhotra, A.(2012):Pediatric non-lymphoblastic non-Hodgkin lymphoma: baseline, interim, and posttreatment PET/CT versus contrast-enhanced CT for evaluation—a prospective study. *Radiology*, 262 (3):956–968.
8. Beanlands, R.S., Nichol, G., Huszti, E., Humen, D., Racine, N., Freeman, M., Gulenchyn, K.Y., Garrard, L., deKemp, R., Guo, A., Ruddy, T.D., Benard, F., Lamy, A., Iwanochko, R.M. and; PARR-2 Investigators.(2007):F-18-fluorodeoxyglucose positron emission tomography imaging-assisted management of patients with severe left ventricular dysfunction and suspected coronary disease: a randomized controlled trial (PARR-2). *J Am. Coll. Cardiol.*, 50(20):2002-2012.
9. Bengel, F.M., Higuchi, T., Javadi, M.S. and Lautamäki, R.(2009): Cardiac Positron Emission Tomography. *J Am. Coll. Cardiol.*, 54(1):1-15.
10. Berman, D.S., Hachamovitch, R., Shaw, L.J., Friedman, J.D., Hayes, S.W., Thomson, L.E., Fieno, D.S., Germano, G., Slomka, P., Wong, N.D., Kang, X. and Rozanski, A.(2006):Roles of nuclear cardiology, cardiac computed tomography, and cardiac magnetic resonance: assessment of patients with suspected coronary artery disease. *J Nucl. Med.*, 47(1):74-82.
11. Bluemke, D.A., Achenbach, S., Budoff, M., Gerber, T.C., Gersh, B., Hillis, L.D., Hundley, W.G., Manning, W.J., Printz, B.F., Stuber, M. and Woodard, P.K.(2008): Noninvasive coronary artery imaging: magnetic resonance angiography and multidetector computed tomography angiography: a scientific statement from the American Heart Association Committee on cardiovascular imaging and intervention of the council on cardiovascular radiology and intervention, and the councils on clinical cardiology and cardiovascular disease in the young. *Circulation*, 118(5):586–606.

12. **Cerqueira, M.D., Weissman, N.J., Dilsizian, V., Jacobs, A.K., Kaul, S., Laskey, W.K., Pennell, D.J., Rumberger, J.A., Ryan, T., Verani, M.S. and American Heart Association Writing Group on Myocardial Segmentation and Registration for Cardiac Imaging.(2002):**Standardization myocardial segmentation and nomenclature for tomographic imaging of the heart: A statement for healthcare professionals from the Cardiac Imaging committee of the Council on Clinical Cardiology of the American Heart Association. *Circulation*,105(4):539–542.
13. **Cheng, G., Servaes, S. and Zhuang, H.(2013):** Value of 18F-fluoro-2-deoxy-D-glucose positron emission tomography/computed tomography scan versus diagnostic contrast computed tomography in initial staging of pediatric patients with lymphoma. *Leuk. Lymphoma*, 54(4):737–742.
14. **Danad, I., Raijmakers, P.G. and Knaapen, P.(2013):** Diagnosing coronary artery disease with hybrid PET/CT: it takes two to tango. *J Nucl. Cardiol.*, 20(5):874–890.
15. **Dorbala, S., Hachamovitch, R., Curillova, Z., Thomas, D., Vangala, D., Kwong, R.Y. and Di Carli, M.F.(2009):**Incremental prognostic value of gated Rb-82 positron emission tomography myocardial perfusion imaging over clinical variables and rest LVEF. *JACC Cardiovasc. Imaging*, 2(7):846-854.
16. **Di Carli, M.F. and Murthy, V.L.(2011):**Cardiac PET/CT for the evaluation of known or suspected coronary artery disease. *Radiographics*, 31(5):1239-1254.
17. **Flotats, A., Knuuti, J., Gutberlet, M., Marcassa, C., Bengel, F.M., Kaufmann, P.A., Rees, M.R., Hesse, B. and Cardiovascular Committee of the EANM, the ESCR and the ECNC.(2011):** Hybrid cardiac imaging: SPECT/CT and PET/CT. A joint position statement by the European Association of Nuclear Medicine (EANM), the European Society of Cardiac Radiology (ESCR) and the European Council of Nuclear Cardiology (ECNC). *Eur J Nucl. Med. Mol. Imaging*, 38(1):201–212.
18. **Furth, C., Denecke, T., Steffen, I., Ruf, J., Voelker, T., Misch, D., Vondran, F., Plotkin, M., Stöver, B., Henze, G., Lemke, A.J. and Amthauer, H.(2006):**Correlative imaging strategies implementing CT, MRI, and PET for staging of childhood Hodgkin disease. *J Pediatr. Hematol. Oncol.*, 28(8):501–512.
19. **Furth, C., Steffen, I.G., Amthauer, H., Ruf, J., Misch, D., Schönberger, S., Kobe, C., Denecke, T., Stöver, B., Hautzel, H., Henze, G. and Hundsdorfer, P.(2009):**Early and late therapy response assessment with [18F] fluorodeoxyglucose positron emission tomography in pediatric Hodgkin's lymphoma: analysis of a prospective multicenter trial. *J Clin. Oncol.*, 27(26):4385–4391.
20. **Fuster, D., Duck, J., Paredes, P., Velasco, M., Muñoz, M., Santamaría, G., Fontanillas, M. and Pons, F.(2008):**Preoperative staging of large primary breast cancer with [¹⁸F] fluorodeoxyglucose positron emission tomography/computed tomography compared with conventional imaging procedures. *J Clin. Oncol.*, 26(29):4746–4751.
21. **Gaemperli, O. and Kaufmann, P.A.(2011):** PET and PET/CT in cardiovascular disease. *Ann N Y Acad Sci.*, 1228(1):109–136.
22. **Gaziano, T.A., Bitton, A., Anand, S., Abrahams-Gessel, S. and Murphy, A (2010):** Growing epidemic of coronary heart disease in low- and middle-income countries. *Curr. Probl. Cardiol.*, 35(2):72–115.
23. **Ghosh, N., Rimoldi, O.E., Beanlands, R.S. and Camici, P.G.(2010):**Assessment of myocardial ischaemia and viability: role of positron emission tomography. *Eur Heart J.*, 31(24):2984–2995.
24. **Groves, A.M., Speechly-Dick, M.E., Kayani, I., Pugliese, F., Endozo, R., McEwan, J., Menezes, L.J., Habib, S.B., Prvulovich, E. and Ell, P.J.(2009):**First experience of combined cardiac PET/64-detector CT angiography with invasive angiographic validation. *Eur J Nucl. Med. Mol. Imaging*, 36(12):2027-2033.
25. **Health.ny.gov.(2015):** 'Basic Statistics: About Incidence, Prevalence, Morbidity, and Mortality - Statistics Teaching Tools - New York State Department of Health'. N.p., 1999. Web. 7 Apr. 2015.
26. **Ilivitzki, A., Radan, L., Ben-Arush, M., Israel, O. and Ben-Barak, A.(2013):** Early interim FDG PET/CT prediction of treatment response and prognosis in pediatric Hodgkin disease: added value of low-dose CT. *Pediatr. Radiol.*, 43(1):86–92.
27. **Jang, B., Park, S., Kang, S.H., Kim, J.K., Kim, S.K., Kim, I.H. and Choi, Y.(2012):** Gold nanorods for target selective SPECT/CT imaging and photothermal therapy in vivo. *Quant Imaging Med Surg.*, 2(1):1–11.
28. **Kabickova, E., Sumerauer, D., Cumlivska, E., Drahekoupilova, E., Nekolna, M., Chanova, M., Hladikova, M., Kodet, R. and Belohlavek, O.(2006):**Comparison of 18F-FDG-PET and standard procedures for the pretreatment staging of children and adolescents with Hodgkin's disease. *Eur J Nucl. Med. Mol. Imaging*, 33(9):1025–1031.
29. **Klocke, F.J., Baird, M.G., Lorell, B.H., Bateman, T.M., Messer, J.V., Berman, D.S., O'Gara, P.T., Carabello, B.A., Russell, R.O. Jr, Cerqueira, M.D., St John Sutton, M.G., DeMaria, A.N., Udelson, J.E., Kennedy, J.W., Verani, M.S., Williams, K.A., Antman, E.M., Smith, S.C. Jr, Alpert, J.S., Gregoratos, G., Anderson, J.L., Hiratzka, L.F., Faxon, D.P., Hunt, S.A., Fuster, V., Jacobs, A.K., Gibbons, R.J., Russell,**

- R.O.; American College of Cardiology; American Heart Association Task Force on Practice Guidelines; and American Society for Nuclear Cardiology.(2003):** ACC/AHA/ASNC Guidelines for the clinical use of cardiac radionuclide imaging-executive summary: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/ASNC Committee to revise the 1995 Guidelines for the clinical use of cardiac radionuclide imaging) *Circulation*,108:1404–1418. *J Am Coll. Cardiol.* **2003**;42:1318–1333.
30. **Levine, J.M., Weiner, M. and Kelly, K.M.(2006):** Routine use of PET scans after completion of therapy in pediatric Hodgkin disease results in a high false positive rate. *J Pediatr. Hematol. Oncol.*, 28:711–714
 31. **Li, Y., Zhang, W., Wu, H. and Liu G.(2014):**Review Article: Advanced Tracers in PET Imaging of Cardiovascular Disease; *BioMed Res Int.*,2014, Article ID 504532, 13 pages <http://dx.doi.org/10.1155/2014/504532>
 32. **Lloyd-Jones, D., Adams, R.J., Brown, T.M., Carnethon, M., Dai, S., De Simone, G., Ferguson, T.B., Ford, E., Furie, K., Gillespie, C., Go, A., Greenlund, K., Haase, N., Hailpern, S., Ho, P.M., Howard, V., Kissela, B., Kittner, S., Lackland, D., Lisabeth, L., Marelli, A., McDermott, M.M., Meigs, J., Mozaffarian, D., Mussolino, M., Nichol, G., Roger, V.L., Rosamond, W., Sacco, R., Sorlie, P., Stafford, R., Thom, T., Wasserthiel-Smoller, S., Wong, N.D., Wylie-Rosett, J. and American Heart Association Statistics Committee and Stroke Statistics Subcommittee.(2010):**Executive summary: heart disease and stroke statistics--2010 update: a report from the American Heart Association. *Circulation*, 121(7): 948-954. Erratum in: *Circulation*. 2010; 121(12):e259.
 33. **Machac, J.(2005):**Cardiac positron emission tomography imaging. *Semin. Nucl. Med.*, 35(1): 17-36.Review.
 34. **Mahon, C.R., Lehman, D.C. and Manuseles, G.(2011):** Textbook of Diagnostic Microbiology. Fifth Edition, Saunders.
 35. **McQuattie, S. (2008):**Pediatric PET/CT imaging: tips and techniques.*J Nucl. Med. Technol.*, 36(4):171-80. doi: 10.2967/jnmt.108.051995. Epub 2008 Nov 13. Review. PMID:19008284
 36. **Meany, H.J., Gidvani, V.K. and Minniti, C.P. (2007):**Utility of PET scans to predict disease relapse in pediatric patients with Hodgkin lymphoma. *Pediatr. Blood Cancer* 48(4):399–402.
 37. **MedCalc, easy-to-use statistical software,(2016):** MedCalc manual, Statistic Menu, ROC Curve Analysis in MedCalc, Version 16.2.1 - Last modified: March 4, 2016 © 1993-2016. MedCalc Software bvba. [https://www.medcalc.org/manual/roc curves.php](https://www.medcalc.org/manual/roc%20curves.php)
 38. **Miller, E., Metser, U., Avrahami, G., Dvir, R., Valdman, D., Sira, L.B., Sayar, D., Burstein, Y., Toren, A., Yaniv, I. and Even-Sapir, E.(2006):**Role of 18F-FDG PET/CT in staging and follow-up of lymphoma in pediatric and young adult patients. *J Comput. Assist Tomogr.*, 30(4):689–694.
 39. **Namdar, M., Hany, T.F., Koepfli, P., Siegrist, P.T., Burger, C., Wyss, C.A., Luscher, T.F., von Schulthess, G.K. and Kaufmann, P.A.(2005):**Integrated PET/CT for the assessment of coronary artery disease: a feasibility study. *J Nucl. Med.*, 46(6):930-935.
 40. **Nekolla, S.G., Martinez-Moeller, A. and Saraste, A.(2009):**PET and MRI in cardiac imaging: from validation studies to integrated applications. *J Nucl Med Mol Imaging*, 36(Suppl 1):S121–S130. DOI 10.1007/s00259-008-0980-1
 41. **Ng, S.H., Chan, S.C., Yen, T.C., Chang, J.T., Liao, C.T., Ko, S.F., Liu, F.Y., Chin, S.C., Fan, K.H. and Hsu, C.L.(2009):**Staging of untreated nasopharyngeal carcinoma with PET/CT: comparison with conventional imaging work-up.*Eur J Nucl Med Mol Imaging*, 36(1):12–22. Epub 2008 Aug 15. Erratum in: *Eur J Nucl. Med. Mol. Imaging*. 2009 Mar; 36(3):538.
 42. **Nyari, T.(2011):** Mathematical and Statistical Modelling in Medicine, Diagnostic Study: Conditional probability. www.model.u-szeged.hu/data/.../Nyari_HU_SRB_03.pdf
 43. **Parikh, R., Mathai, A., Parikh, S., Chandra Sekhar, G. and Thomas, R.(2008):** Understanding and Using Sensitivity, Specificity and Predictive Values. *Indian J Ophthalmol.*,56(1):45-50.
 44. **Paulino, A.C., Margolin, J., Dreyer, Z., The, B.S. and Chiang, S.(2012):** Impact of PET-CT on involved field radiotherapy design for pediatric Hodgkin lymphoma. *Pediatr Blood Cancer*, 58(6):860–864.
 45. **Peacock, J. and Peacock, P.(2011):**Oxford Handbook of Medical Statistics.Oxford Medical Handbooks. Chapter 9, pp. 342 Oxford University Press.United Kingdom.
 46. **Punwani, S., Taylor, S.A., Bainbridge, A., Prakash, V., Bandula, S., De Vita, E., Olsen, O.E., Hain, S.F., Stevens, N., Daw, S., Shankar, A., Bomanji, J.B. and Humphries, P.D.(2010):**Pediatric and adolescent lymphoma: comparison of whole-body STIR half-Fourier RARE MR imaging with an enhanced PET/CT reference for initial staging. *Radiology*, 255(1):182–190.

47. **Ratib, O. and Nkoulou, R.(2014):** Potential applications of PET/MR imaging in cardiology. *J Nucl. Med.*, 55(Supplement 2):40S-46S.
48. **Riad, R., Omar, W., Kotb, M., Hafez, M., Sidhom, I., Zamzam, M., Zaky, I. and Abdel-Dayem, H.(2010):**Role of PET/CT in malignant pediatric lymphoma. *Eur J Nucl. Med. Mol. Imaging*, 37(2):319–329.
49. **Rispler, S., Keidar, Z., Ghersin, E., Roguin, A., Soli, A., Dragu, R., Litmanovich, D., Frenkel, A., Aronson, D., Engel, A., Beyar, R. and Israel, O.(2007):**Integrated single photon emission computed tomography and computed tomography coronary angiography for the assessment of hemodynamically significant coronary artery lesions. *J Am Coll. Cardiol.*, 49(10):1059–1067.
50. **Sato, A., Nozato, T., Hikita, H., Miyazaki, S., Takahashi, Y., Kuwahara, T., Takahashi, A., Hiroe, M. and Aonuma, K.(2010):**Incremental value of combining 64-slice computed tomography angiography with stress nuclear myocardial perfusion imaging to improve noninvasive detection of coronary artery disease. *J Nucl Cardiol.*, 17(1):19-26.
51. **Schiller, N.B., Shah, P.M., Crawford, M., DeMaria, A., Devereux, R., Feigenbaum, H., Gutgesell, H., Reichek, N., Sahn, D., Schnittger, I. and et al.(1989):** Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. *J Am Soc Echocardiogr.*, 2(5):358–367.
52. **Schinkel, A.F., Bax, J.J., Poldermans, D., Elhendy, A., Ferrari, R. and Rahimtoola, S.H.(2007):**Hibernating myocardium: diagnosis and patient outcomes. *Curr. Probl. Cardiol.*, 32(7):375–410. Review.
53. **Schwaiger, M., Ziegler, S. I. and Nekolla, S. G.(2010):**PET/CT challenge for the non-invasive diagnosis of coronary artery disease. *Eur J Radiol.*, 73(3):494–503. Review.
54. **Sogbein, O.O., Pelletier-Galarneau, M., Schindler, T. H., Wei, L., Wells, R. G. and Ruddy, T.D.(2014):**New SPECT and PET radiopharmaceuticals for imaging cardiovascular disease. *BioMed. Res Int.*, 2014: 942960. 25 pages. doi: 10.1155/2014/942960. Epub 2014 May 11.
55. **Souvatoglou, M., Bengel, F., Busch, R., Kruschke, C., Fernolendt, H., Lee, D., Schwaiger, M. and Nekolla, S.G.(2007):**Attenuation correction in cardiac PET/CT with three different CT protocols: a comparison with conventional PET. *Eur J Nucl. Med. Mol. Imaging*, 34(12):1991–2000.
56. **Strobel, K., Skalsky, J., Kalff, V., Baumann, K., Seifert, B., Joller-Jemelka, H., Dummer, R. and Steinert, H.C.(2007):**Tumour assessment in advanced melanoma: value of FDG PET/CT in patients with elevated serum S-100B. *Eur J Nucl. Med. Mol. Imaging*, 34(9):1366–1375.
57. **Sun, Z.(2013):** Cardiac Imaging Modalities in the Diagnosis of Coronary Artery Disease. *J Clin. Exp. Cardiol.*, S6:e001. <http://dx.doi.org/10.4172/2155-9880.S6-e001>
58. **Sun, Z.H., Cao, Y. and Li, H.F.(2011):**Multislice computed tomography angiography in the diagnosis of coronary artery disease. *J Geriatr. Cardiol.*, 8(2):104-113.
59. **Troost, E.G.C., Schinagl, D.A.X., Bussink, J., Boerman, O.C., van der Kogel, A.J., Oyen, W.J.G. and Kaanders, J.H.A.M.(2015):**Innovations in Radiotherapy Planning of Head and Neck Cancers: Role of PET. *J Nucl. Med.* 2015, Print ISSN: 1540-1405. Online ISSN: 1540-1413. Copyright © 2015 by Journal of the National Comprehensive Cancer Network. *J Nucl. Med.* 2010;51(1):66-76. doi: 10.2967/jnumed.108.061499. Epub 2009 Dec 15.
60. **Underwood, S.R., de Bondt, P., Flotats, A., Marcasa, C., Pinto, F., Schaefer, W. and Verberne, H.J.(2014):** The current and future status of nuclear cardiology: a consensus report. *Eur Heart J Cardiovasc Imaging*, 15(9):949-55. doi: 10.1093/ehjci/jeu060. Epub 2014 May 12.
61. **Uslu, L., Doing, J., Link, M., Rosenberg, J., Quon, A. and Daldrup-Link, H.E.(2015):**Value of 18F-FDG PET and PET/CT for evaluation of pediatric malignancies. *J Nucl Med.*, 56(2):274–286. DOI: 10.2967/jnumed.114.146290
62. **Veit-Haibach, P., Vogt, F.M., Jablonka, R., Kuehl, H., Bockisch, A., Beyer, T., Dahmen, G., Rosenbaum, S. and Antoch, G.(2009):**Diagnostic accuracy of contrast-enhanced FDG PET/CT in primary staging of cutaneous malignant melanoma. *Eur J Nucl Med Mol Imaging*, 36(6):910–918.
63. **von Schulthess, G.K., Steinert, H.C. and Hany, T.F.(2006):** Integrated PET/CT: current applications and future directions. *Radiology*, 238(2):405–422.
64. **Weber, W.A.(2005):** Use of PET for monitoring cancer therapy and for predicting outcome. *J Nucl Med.*, 46(6):983–995. Review.
65. **Xu, G., Zhao, L. and He Z.(2012/2015):**Performance of Whole-Body PET/CT for the Detection of Distant Malignancies in Various Cancers: A Systematic Review and Meta-Analysis. *Journal of Nuclear Medicine* Print ISSN: 0161-5505. Online ISSN: 2159-662X Copyright © 2015 Society of Nuclear Medicine and Molecular Imaging. *J Nucl Med.*, 53(12):1847-54. doi: 10.2967/jnumed.112.105049. Epub 2012 Oct 16.