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Research Article

The Role of Positron Emission Tomography - Computed Tomography (PET - CT) Scan in the Assessment and Management of Carcinoma of the Prostate Gland: A Review and Update

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Abstract

Background: PET CT Scan has been used on numerous occasions in the assessment and management of various malignancies but it is only occasionally used in the assessment management of carcinoma of the prostate gland globally. There is the need to establish whether or not PET/CT scan is a useful imaging technique which should be used more often in the investigation of biochemical failure following treatment of carcinoma of prostate gland with curative intent

Aim: To investigate the suggestion that PET/CT scan would be a useful and reliable imaging option for the investigation of biochemical recurrence resulting following the treatment of prostate cancer with curative intent by reviewing the literature relating to the use of PET / CT scan in carcinoma of the prostate gland.

Method: Various internet data bases were searched including: Google, Google Scholar, Yahoo, and PUBMED. The search words that were used included: PET/CT Scan in carcinoma of the prostate, PET/CT scan in prostate cancer, PET/CT scan and prostate cancer, PET/CT scan and carcinoma of the prostate.

Results: Fifty two manuscripts that have been published relating to the use of a form of PET/CT scan in relationship to investigation of carcinoma of the prostate gland were utilized to write the article. One of the articles published in Dutch was a review article. Another paper reported the use of PET CT scan in the diagnosis of Hurtle tumour (a benign tumour) in association with carcinoma of the prostate gland. The remaining manuscripts contained case reports and studies regarding the use of various types of PET/CT scan in the investigation of biochemical failure as well as in the treatment and follow-up of some cases of metastasis. On the whole almost all of the papers had confirmed the high sensitivity and high specificity of PET/CT scan in detecting localized and distant metastatic lesions in the scenario of slight elevations of serum PSA. There have been reports of PET/CT scan being able to detect localized and distant metastasis when conventional computed tomography scan and isotope bone scan failed to detect metastases. In one case when the serum PSA level was high isotope bone scan and CT scan failed to detect bone metastases but PET/CT scan detected bone metastases.

Conclusions: PET/CT Scan is a very useful imaging modality that detects localized and distant metastases in biochemical recurrence of prostate cancer and this modality of imaging should be used more often from now onwards. CT scan would usually detect nodes/lesions that measure 1 cm or larger but PET/CT scan would detect smaller sized lesions at slightly raised levels of serum PSA. The detection of small localized metastasis at a slightly elevated serum PSA values would make it easier for the undertaking of a second-line treatment of curative intent in the form of salvage lymphadenectomy or salvage radiotherapy targeted at the lesion. Perhaps PET/CT scan should be the first-line imaging modality which should be used in investigating biochemical recurrence and this should be done when the serum PSA is slightly elevated.

Key Words: Positron emission tomography scan; carcinoma of prostate; biochemical recurrence; isotope bone scan, computed tomography scan; magnetic resonance imaging scan; radical prostatectomy; radical external beam radiotherapy; brachytherapy; Serum prostatic-specific antigen.

Introduction

Carcinoma of the prostate gland is stated to represent the second most frequent malignant tumour after lung cancer that tends to be encountered globally in men as well as carcinoma of the prostate gland does account for 1,276,106 new cases and it has caused 358,989 deaths which had amounted to 3.8% of all deaths that had been caused by carcinoma in men in 2018 [1, 2, 3]. it has been iterated that the incidence as well as the mortality associated with carcinoma of the prostate gland globally do correlate with increasing age with the average age at the time of the initial diagnosis of the malignancy being 60 years [1]. It has been noted that with regard to African-American men, the incidence rates tend to be higher in comparison with white men, with 158.3 new cases of carcinoma of the prostate gland diagnosed per 100,000 men and their mortality is about twice in the African-American as in White men [4]. The reasons related to this disparity has been postulated to relate to differences in social, environmental, as well as genetic factors [1]. It has been iterated that even though 2,293.818 new cases of carcinoma of the prostate gland are estimated to be encountered until 2040, a small variation with regard to mortality related to carcinoma of the prostate gland will be observed which would represent an increase of 1.05% [5]. It has been iterated that carcinoma of the prostate gland could be asymptomatic within the early stage of the malignancy as well as quite often carcinoma of the prostate gland does tend to portend an indolent course as well as the carcinoma of the prostate gland could require minimal treatment or no treatment at times. [1]. Nevertheless, the most frequent presentation of carcinoma of the prostate gland has tended to be frequent complaint of difficulty with micturition, urinary voiding frequency, as well as nocturia, which are all symptoms that could also arise from benign hypertrophy of the prostate gland [1]. It has also been iterated that more advanced stage of carcinoma of the prostate could manifest with retention of urine, as well as back pain, in view of the fact that the axial skeleton tends to be the commonest site for the development of bone metastases [1]. Many cases of carcinoma of the prostate gland had been identified or diagnosed based upon the finding of raised serum levels of prostate-specific antigen (PSA), with a serum PSA level higher than 4 ng / ML, which is a glycoprotein that is normally expressed by the tissue of the prostate gland [1]. It has also been iterated that in view of the fact that some men who do not have carcinoma of the prostate gland have been found to have raised serum levels of PSA, the undertaking of a tissue biopsy has remained the standard of care that does confirm the diagnosis of carcinoma of the prostate gland based upon pathology examination of the biopsy specimen [1]. It has also been stated that diet and physical activity do play a pivotal role with regard to the development as well as progression of carcinoma of the prostate gland [1]. It has additionally been iterated that dietary factors tend usually to be associated with the observed global as well as ethnic differences in the incidence rates of carcinoma of the prostate gland [6-10]. A few decades ago when many centres in the world did not have facilities for radiology imaging-guided biopsy of the prostate gland especially within some of the developing countries, biopsies of the prostate gland were undertaken based upon the finding of nodules on the prostate gland, hardness of the prostate gland, or abnormalities of the prostate gland and biopsies of the prostate gland were undertaken via the trans-rectal or trans-perineal route based upon the guidance of finger examination of the prostate gland. With developments in radiology imaging including ultrasound scan, computed tomography scan, and magnetic resonance imaging scan, radiology imaging-guided biopsies of the prostate gland (ultrasound scan-guided -, CT scan-guided-, and MRI scan-guided-biopsies) have developed and these tend to undertaken by means of the trans-rectal route, and trans-perineal route as well as the undertaking of targeted biopsies of abnormal sites of the prostate gland that have been found upon radiology imaging are now being undertaken in the initial assessments of prostate gland in order to establish the diagnosis of carcinoma of the prostate gland. With the finding of carcinoma of the prostate gland the initial full staging of the prostate gland has been undertaken by means of computed tomography (CT) scan of the thorax, abdomen, and pelvis. Magnetic resonance Imaging (MRI) scan of the thorax, abdomen, and pelvis can also be used for the initial staging of a newly diagnosed carcinoma of the prostate gland. Within some parts of the developing world where CT scans and MRI scans are not available in many district hospitals, chest x-ray and ultrasound scans have tended to be utilized in the initial staging of a newly diagnosed carcinoma of the prostate gland before patients are then referred on to tertiary centres within cities of these countries. When patients have undergone treatment of curative intent for localized carcinoma of the prostate gland by means of radical prostatectomy or radical radiotherapy (external beam radiotherapy or brachytherapy), they tend to be followed-up with the undertaking of regular follow-up computed tomography (CT) scans, or magnetic resonance imaging (MRI) scans of the thorax, abdomen, and pelvis. In areas of the world where CT scan machines and MRI scan machines are not readily available or they are too expensive for patients who are undergoing follow-up assessments following treatment of carcinoma of the prostate gland, chest radiograph and ultrasound scan of abdomen and pelvis are being undertaken in the follow-up assessments of patients who have undergone treatment of curative intent for carcinoma of the prostate gland. In order to exclude the possibility of bone metastases, isotope bone scans tend to be undertaken as well as CT scan or MRI scan. All individuals who undergo treatment for carcinoma of the prostate gland also have regular serum prostate-specific antigen (PSA) taken and when there is evidence of biochemical failure, CT scan and or MRI scan of thorax, abdomen, and pelvis tend to be undertaken to ascertain the site or sites of the local recurrent tumour or metastatic lesion. In the initial stages of biochemical failure pursuant to treatment of curative intent of localized carcinoma of the prostate gland, CT scan and MRI scan would tend not to identify small or microscopic localized recurrent prostate cancer or small metastatic prostate cancer in some cases of biochemical (PSA) recurrence. It does appear that the undertaking of positron emission tomography scan does identify small local recurrent and small metastatic carcinomas of the prostate gland which conventional CT scan and conventional MRI scan cannot identify. Conventional radiology imaging with the undertaking of computed tomography (CT) scan, magnetic resonance imaging (MRI) scan, and isotope bone scan tends to be limited with regard to the identification of nodal as well as distant bone metastases in cases of carcinoma of the prostate gland. Furthermore, advances have been made with regard to available treatment options for the treatment of localized recurrent tumour and systemic / metastatic disease, which do drive forward the requirement for the utilization of precise diagnostic as well as prognostication in order to refine the individual approaches to treatment at various times in the management of carcinoma of the prostate gland. Positron emission tomography (scan) does play an evolving role with regard to the assessment of carcinoma of the prostate gland, especially with regard to the scenario of biochemical recurrence (biochemical relapse). Additionally, many studies have been devoted the genes that are involved in the inherited form of carcinoma of the prostate gland as well as the mutations that occur within the acquired form of carcinoma of the prostate gland. The ensuing literature on the use of PET/CT scan in carcinoma of the prostate gland is divided into two parts: (A) Overview and (B) Miscellaneous narrations and Discussions from some reported cases, case, as well as studies on the use of PET/CT scan in carcinoma of the prostate gland.

Methods

Various internet data bases were searched including: Google, Google Scholar, Yahoo, and PUBMED. The search words that were used included: PET/CT Scan in carcinoma of the prostate, PET/CT scan in prostate cancer, PET/CT scan and prostate cancer, PET/CT scan and carcinoma of the prostate. Fifty two references were identified which were used to write the article which has been divided into two parts (A) Overview and (B) Miscellaneous narrations and discussions from case

reports, case series, and studies related to PET/CT scan and prostate cancer.

Result / Review and Update of the Literature.

(A) Overview

Definition and general statements

- Positron Emission Tomography-Computed Tomography scan which quite often is referred to as PET-CT scan or PET/CT scan is a terminology that refers to a nuclear medicine procedure that combines, in a single gantry, a positron emission tomography (PET) scanner as well as X-ray computed tomography (scanner), in order to acquire sequential radiology images from both devices contemporaneously within the same session are then combined into a single super-imposed, co-registered image [11].
- The functional images that are obtained from PET scanning that illustrate the spatial distribution of the metabolic activity or biochemical activity within the body could be more precisely aligned or correlated with the anatomic images that have been produced by computed tomography (CT) scanning [11].
- Two- and three-dimensional reconstruction of image could be rendered as a function of a common software as well as control system [11].
- It has been iterated that utilization of PET-CT scan has been responsible for revolution in the medical diagnosis of many conditions in many various medical fields and that PET-CT has added precision of anatomical localization of various medical diseases to functional imaging of various medical lesions/diseases which had previously been lacking with regard to pure computed tomography (CT) imaging [11].
- Various diagnostic imaging investigations in various procedures including oncology procedures, planning of surgical management, radiotherapy, and staging of carcinomas have changed quickly based upon the influence of the availability of positron emission tomography-computed tomography scanning devices as well as some radiology departments are stated to have slowly abandoned the conventional PET devices and they are substituting the PET devices for PET-CT scan devices [11].
- It has been iterated that even though the combined/hybrid PET/CT scan device tends to be more expensive in comparison with the PET scanner or CT scanner, the PET/CT scanner does have the advantage of providing both functions of a PET scanner and a CT scanner as standalone examinations because the PET/CT scanner represents two devices standing alone as one device [11].
- Some of reasons why there is at the moment lack of wide utilization of PET-CT scanners include (a) the difficulty of producing PET/CT scanners, (b) the cost of production of a PET/CT scanner as well as the high cost of transportation the radiopharmaceuticals that are utilized for the PET imaging and the fact that the radiopharmaceuticals tend to be very short-lived, taking into consideration the half-life of the radioactive Fluorine-18 (18F) which is utilized to trace glucose metabolism with utilization of fluorodeoxyglucose, FDG, lasts only two hours. The production of FDG does require a very expensive cyclotron as well as the production line for the radiopharmaceuticals for PET-MRI scan like PET-CT scan does combine modalities to produce co-registered images which are expensive for general use in most small district hospitals and even some tertiary hospitals especially in developing countries [11].
- Some of the conditions for which PET/CT scanners are used include:
  - Breast cancer [12].
  - Planning of surgical operation for example head and neck cancer [13].
  - Oncology assessments [14]
  - Radiotherapy procedures and planning [15]
  - Staging of Malignancies [16]
  - Assessment of Biochemical failure after radical prostatectomy or radiotherapy for prostate cancer. [17]

History

- It has been iterated that the combination of Positron Emission Tomography (PET) and Computed tomography (CT) scanners was first suggested by R Raylman in his Doctor of Philosophy (PHD) thesis in 1991 [1,18].
- It has also been iterated that the first Positron Emission Tomography – Computed Tomography (PET-CT) systems were constructed by David Townsend within the University of Geneva at the time as well as by Ronald Nutt at CPS Innovations in Knoxville, TN, with help that was provided by colleagues. [2,19,20]
- It has been documented that the first PET-CT prototype for utilization for clinical evaluative assessment had been funded by the NCI and this was installed within the University of Pittsburgh Medical Centre in 1998 [19].
- It has been iterated that the first commercial system of PET-CT scanners reached the market by 2001, and by 2004, more than 400 PET-CT scanner systems had been installed globally Following this several PET-CT scanners have been installed in many hospitals globally; nevertheless, there are many hospitals globally that do not have PET-CT scanners, especially within the developing countries in which there are very few radiologists.

Recent summations related to ^{18}F-NaF PET/CT scan:

- It has been iterated that on the whole ^{18}F-NaF PET/CT scan is a sensitive radiological imaging option for the detection of bone metastases with regard to patients who have carcinoma of the prostate gland and it could be utilized for the diagnosis of the prostate cancer at staging [22,23]
- Nevertheless, ^{18}F-NaF PET/CT has not been recommended by the EAU guidelines for routine utilization, in view of the fact that ^{18}F-NaF PET/CT does not assess soft tissue as well as 1^{18}F-NaF PET/CT has limited specificity [24].
- Additionally, despite higher diagnostic performance and higher quality images, with a shorter acquisition time in comparison with Tc-labelled phosphonate bone scan, utilization of ^{18}F-NaF PET/CT has been limited by its financial cost as well as availability in view of availability of PET for general use in most radiology departments [22].
- It has been pointed out that ^{18}F-NaF PET/CT does have superior diagnostic performance with regard to the identification of bone metastases, in comparison with ^{99m}Tc-labeled phosphonate bone scan; nevertheless, utilization of ^{18}F-NaF PET/CT has been limited by a relative lack of specificity in comparison with the specificity of other Pet tracers, and it does not allow for the assessment of soft tissue [22].

Concluding summations and Recommendations made at the 2016 RSNA Education Annual Meeting Presentation. (Salient points obtained from an educational exhibit at the 2016 RSNA Annual Meeting) include: [22]

- During the preceding decade, rapidly growing research into various PET tracers had emerged [22].
- The utilization of functional radiology imaging with PET tracers that target a variety of aspects of the natural tumour biology of carcinoma of prostate gland had shown superior detection in comparison with utilization of conventional radiology imaging with utilization of computed tomography (CT) scan, magnetic resonance imaging (MRI) scan, or bone scan [22].
- A particular strength that is associated with utilization of PET imaging relates to the early identification of disease with regard to patients who develop biochemical relapse, which represents a strength that gives the clinician the opportunity for a personal approach or precision medical treatment with the undertaking of localized salvage treatment or the treatment of oligometastatic disease, with the intention of providing possible treatment of curative intent or cure or improved outcomes [22].
- The NCCN guidelines do suggest that choline PET/CT could be taken into consideration with regard to patients who develop biochemical failure (biochemical relapse) [23]; nevertheless, the detection rates tend to vary based upon the serum prostate specific antigen (PSA) level; thus the EAU guidelines have recommended the utilization of choline PET/CT for patients whose serum PSA levels are 1 ng/mL or higher than 1 ng / mL, pursuant to radical prostatectomy, and multi-parametric Magnetic resonance (MR) imaging pursuant to radical radiotherapy [24].
- 68Ga-PSMA does detection rates with regard to patients who develop biochemical relapse, with higher detection rates and higher tumour-to-background ratios in comparison with those with choline, even at low levels of serum PSA. Utilization of 68Ga-PSMA has been supported by the results of multiple relatively recent studies and it had recently been recommended by the European Association of Urology (EAU) for cases of biochemical relapse at serum PSA levels of 1 ng/mL or higher than 1 ng/mL pursuant to radical prostatectomy in order to guide salvage treatment [24].
- The results obtained from initial studies with utilization of 18F-fluciclone did suggest that it is superior to 11C-choline, and it is associated with a favourable biodistribution as well as with relatively less urinary excretion. The PET tracers FDG, 11C-choline, 18F-choline, as well as 68Ga-PSMA are all susceptible to pitfalls of imaging interpretation from urinary physiological activity. An additional post-micturition pelvic acquisition, which tends to be obtained for 18F-choline and 68Ga-PSMA PET/CT in some institutions could help [22].
- 18F-NaF PET scan is superior in comparison with bone scan even SPECT/CT imaging; nevertheless, 18F-NaF PET tends to be limited by its relative lack of specificity in comparison with other PET tracers, by its cost, as well as its availability. Furthermore, 18F-NaF tracer activity tends to be commonly seen in cases of degenerative disease, especially in the older population. Non-specificity of tracer activity has also been demonstrated by PET tracers, despite their more specific molecular targets related to carcinoma of the prostate gland. Activity has also been observed in related and non-related pathology conditions, as well as in benign and malignant pathological conditions, with these tracers [22].
- The cost-effectiveness of PET, in comparison with that of conventional radiology imaging does remain to be determined. Furthermore, not all of the aforementioned tracers tend to be readily available. FDG is said to be the most widely available and it tends to be the commonly utilized tracer with regard to the oncology setting; nevertheless, FDG does have limited utility in cases of carcinoma of the prostate gland in view of the low glucose metabolism of most tumours. With regard to certain clinical settings, FDG could be beneficial, for example, in the response assessment of osseous disease in metastatic castrate-resistant carcinoma of the prostate gland as well as a prognostic indicator [22].
- Further research into the identification of the optimal clinical utility of these PET tracers as well as their cost-effectiveness is awaited and it will likely be reflected in the clinical guidelines that are made in the future [22].

(B) Miscellaneous narrations and discussions from reported cases, case series and various studies on the use of PET/CT Scan in carcinoma of the prostate gland

Ceci et al. [25] evaluated the usefulness of 11 C-choline PET/CT scan in patients who have recurrent carcinoma of the prostate gland and hormone sensitive disease that had been treated by intermittent anti-androgen treatment regime. Ceci et al. retrospectively evaluated 10 patients pursuant to having had radical prostatectomy in the case of 8 patients and after having had external beam radiotherapy for curative intent as primary treatment. All of the ten patients had undergone sequential 11 C-choline PET/CT scans. The first PET/CT (PET1) was undertaken during an anti-androgen therapy (ADT) and the second PET/CT scan (PET2) was undertaken following interruption of the anti-androgen therapy. It was only patients who had negative results in the PET1 were included in the study. At the time of performing PET1 all the patients were undergoing anti-androgen therapy from at least 6 months and their mean serum PSA was 0.54 ng / m L. At the time of performing PET2 all the patients had completed their anti-androgen therapy for a mean period of 7 months. The 11 C-choline PET/CT scan findings had been validated by a follow-up of at least a minimum of 12 months or by histological confirmation of diagnosis in the case of local recurrence. With regard to the results Ceci et al. [25] reported that PET2 was able to detect the site of recurrence in all cases and that at the time of PET2 scanning the mean serum PSA was 3.88 ng / m L as well as the mean serum PSA doubling time (PSAdt) was 2.46 months. Furthermore, the mean serum PSA velocity (PSAvel) was 6.94 ng / mL / year. Four out of the ten patients had a single lesion, 5 out of the ten patients had PET2 scan evidence of 2 lesions and 1 patient had multiple lymph node lesions on the PET2 scan. Ceci et al. [25] made the following conclusions.

- When performed during interruption of ant-androgen therapy, 11 C-choline PET/CT scan had been able to identify the site of tumour recurrence during a rising serum PSA level detection.
- Within this context 11 C-choline PET/CT scan could help in the assessment of the burden of disease or in the change of therapeutic approach by the use of more aggressive and addressed therapies like guided radiotherapy or salvage lymph node dissection.

Souvatzouglou et al. [26] evaluated the performance of conventional [(11)C]choline PET/CT scan in comparison with PET/MRI scan in carcinoma of the prostate gland. Souvatzouglou et al [26] studied 32 patients who had carcinoma of the prostate gland and who had undergone a single-injection dual-imaging protocol with PET/CT scan and subsequent PET/MRI scan. The PET/CT scans were undertaken applying standard clinical protocols (5 minutes pursuant to injection of 793 ± 69Mbq [(11) C] choline, 3 minutes per bed, intravenous contrast agent). Subsequently (52±15 minutes after injection) PET/MRI scan was undertaken (4 minutes per bed position). The PET images had been

reconstructed iteratively (OSEM 3D), scatter and attenuation correction of emission data and regional allocation of [(11)C]choline foci were undertaken using CT data for PET/CT scan and a segmental Dixon MRI, T1 and T2 sequences for PET/MRI scan. The image quality of the respective PET scans as well as PET alignment with the respective morphological imaging modality had been compared with the use of a four point scale (0 to 3). Additionally, the number, the location, and conspicuity of the detected lesions had been evaluated. The SUvs for suspicious lesions, lung, liver, spleen, vertebral bone, and muscle were compared. With regard to the results, Souvatzouglou et al. [26] reported that 80 lesions overall had been scored visually in 29 out of the 32 patients. No significant difference was found between the two scans with regard to the number or conspicuity of the identified lesions (P not significant). PET/MRI scan had T1 and T2 sequences performing better than PET/CT scan in anatomical allocation of the lesions (2.87 ± 0.3 versus 2.72 ± 0.5: P = 0.05). The quality of PET/CT images (2.97 ± 0.2) had been better in comparison with that of the respective Pet scan of the PET/MRI scan (2.69± 0.5; P = 0.007). On the whole the maximum and mean lesional SUVs did exhibit high correlations between PET/CT scan and PET/MRI scan (P = 0.87, and P = 0.86, respectively; both P < 0.001). Souvatzouglou et al. [26] made the following conclusions:

- Despite the fact of a substantially later imaging time-point, the undertaking of simultaneous PET/MRI was comparable with that of PET/CT scan in the detection of lesions with increased [(11)C] choline uptake in patients who have carcinoma of the prostate.
- The anatomical allocation of lesions was found to be better with simultaneous PET/MRI scan in comparison with PET/CT scan especially in bone and in the pelvis
- These promising findings would suggest that [(11)C] choline PET/MRI scan might have a diagnostic benefit in comparison with PET/CT scan in patients who have carcinoma of the prostate gland, and now needs to be evaluated in prospective trials.

Kang et al. [27] evaluated the clinical value of incidental prostate 18FFDG uptake in PET/CT scans. Kang et al. [27] reviewed the 18F-FDG PET/CT scan reports from September 2009 to September 2013 and they selected cases that had been reported to have shown focal/diffuse FDG uptake in the prostate gland. Kang et al. [27] analysed the correlation between 18F-FDG PET/CT scan finding and data which had been collected during evaluations including serum prostate specific antigen, digital rectal examination (DRE) findings, trans-rectal ultrasound scan of prostate (DRE) findings, and or pathological reports of biopsy of prostate to confirm carcinoma of the prostate gland. Out of a total of 18,393 cases 106, (0.6%) did exhibit abnormal hyper-metabolism prostate gland. Additional evaluations were undertaken in 66 patients. Serum prostate-specific antigen (PSA) were found not to be significantly correlated with maximum standardized uptake values (SUV max) in all patients (rho 0.483; P = 0.132). Biopsies of the prostate gland were undertaken in 15 patients, and carcinoma of the prostate gland was confirmed in 11 patients. The median serum PSA level was 4.8 (range 0.55 – 7.06) ng / m L, and 127.4 (1.06 – 495) ng / m L, in the benign and the carcinoma of prostate groups respectively. The median SUVmax was higher in the carcinoma of prostate gland group (mean 10.1, range 3.8 to 24.5) than in the benign group (mean 4.3, range 3.1 to 8.8), but the difference was found not to be statistically significant (P = 0.078). No significant correlations were found between SUVmax, and serum PSA levels, prostate volume or Gleason grade. 18F-FDG PET/CT scan was found not to reliably differentiate malignant, or benign from abnormal uptake lesions within the prostate gland, and routine prostate biopsy had not been routinely recommended who had abnormal FDG uptake. However, Kang et al. [27] recommended that patients who had incidental prostate uptake on 18F-FDG PET/CT scans should not be ignored and they should undergo further evaluations in the form of serum PSA level determinations and digital rectal examinations. .

Hodolic et al. [28] reported a 59-year-old man who had presented with urinary frequency. Six months prior to his presentation, his serum prostate-specific antigen (PSA) level was 1.56 ng / m L and at the time of his current presentation his serum PSA level was 3.5 ng / mL (PSA doubling time 6 months; PSA velocity = 0.19 ng/mL per month). Histological examination of his prostate biopsy showed features consistent with Gleason 5+5 = 10 adenocarcinoma of the prostate gland. He underwent staging of his tumour by having (18)F-fluorocholine PET/CT scan ((18)F-FCH PET/CT) which showed lymph node metastasis. Following six months of having hormonal treatment with goserelin, his serum PSA level had decreased to 0.38 ng / m L. He then had (18) F-FCH PET/CT re-staging scan which showed a global reduction of (18) F-FCH lesion uptake with the disappearance of some mediastinal lymph node activity and iliac as well as pelvic lymph node activity.

Vargas et al. [29] undertook a retrospective study to compare the features of bone metastases at computed tomography (CT) to tracer uptake at fluorine 18 fluorodeoxyglucose (FDG) positron emission tomography (PET) and fluorine 18 16β-fluoro-5-dihydrotestosterone (FDHT) PET and to ascertain the association between these imaging characteristics and the overall survival in men who have castration-resistant carcinoma of the prostate gland. In this study, two readers independently evaluated computed tomography (CT) scans, FDG PET scans, and FDHT PET scans of 38 patients for features of bone metastases. The associations between imaging findings and the overall survival of the patients were determined by utilizing univariate Cox proportional hazards regression. With regard to the results, Vargas et al. [29] reported that reader 1 detected in 38 patients, 881 lesions and reader 2 detected 867 lesions. They found that attenuation coefficients at computed tomography scanning had correlated inversely with FDG (reader 1: r = -0.3007); P < 0.001; reader 2: r = -0.3147, P < 0.001) and FDHT (reader 1: r = -0.2680; P = 0.001, reader 2: r = -0.3656; P < 0.001) uptake. The number of lesions on the CT scans was significantly associated with the overall survival of the patients (reader 1: hazard ratio [HR] 1.025; P = 0.05; reader 2: hazard ratio [HR] 1.021; P = 0.04). The numbers of lesions on the FDG and the FDHT PET scans were found to be significantly associated with survival by reader 1 (hazard ratio [HR] 1.051 – 1.109, P < 0.001; and also significantly associated with survival by reader 2 (hazard ratio [HR] 1.026 1.082; P ≤ 0.009). The patients who had higher FDHT uptake (lesion with the highest maximum standardized uptake value) did have significantly shorter survival (reader 1: hazard ratio [HR] 1.078; P = 0.02; reader 2: hazard ratio [HR] 1.092; P = 0.02). FGD uptake intensity was found not to be associated with overall survival of the patients (reader 1: P = 0.65; reader 2: P = 0.38). Vargas et al. [29] concluded that in patients who have castrate resistant carcinoma of the prostate gland, the numbers of bone lesions on CT scan, FDG PET/CT scan, and FDHT PET/CT scan and the intensity of the FDHT uptake tend to be significantly associated with the overall survival of the patients.

Buchegger et al. [30] reported the results of a comparative, prospective PET/CT scan study of both tracers that had been in the same patients who had developed recurrence of their carcinoma of the prostate and low serum PSA in order to compare the diagnostic information provided by the two tracers. Buchegger et al.[30] stated that they had studied 23 patients who had developed rising serum PSA following treatment of curative intent. Seven patients had undergone radical prostatectomy and subsequently developed rising serum PSA ≤ 3 ng / m L; 7 patients had undergone radiotherapy of curative intent and subsequently developed rising serum PSA 0f ≤ 5 ng / m L; 9 patients had undergone radical prostatectomy and salvage radiotherapy and subsequently developed rising serum PSA levels of ≤ 5 ng / m L. Both FCG and ACE PET/CT scans were undertaken on all patients in a random sequence with a mean

of 4 days and a range of 0 to 11 days apart. FCH PET/CT scan was started at injection (307 ± 16 MBq) with a 10 minutes dynamic acquisition of the prostate bed ensued by a whole-body PET scan and late (45 minutes later) imaging of the pelvis. ACE PET/CT scan was undertaken as double whole-body PET scan starting 5 minutes and 22 minutes after following the injection (994 ± 72 MBq) , and a late view (45 minutes later) of the prostate bed. The PET/CT scans had been blindly reviewed by two independent pairs of two experienced nuclear medicine physicians, and discordant sub-group results were discussed to obtain consensus for positive, negative, or equivocal results. With regard to the results, Buchegger et al. [30] reported that the PET results had been concordant in 88 out of 92 local, regional, and distant findings (Cohen's kappa 0.929). The results were adjudged to be concordant in all of the patients with regard to local status, bone metastases, and distant findings. Buchegger et al. [30] also reported that the lymph node results had been concordant in 19 patients and different with regard to 4 patients. With regard to per patient basis, the results were found to be concordant in 22 out of 23 patients (14 positive, 5 negative, and 3 equivocal). However, in one patient ACE PET/CT scan was positive for nodal metastasis and whilst FCH PET/CT scan was overall negative. Furthermore, interestingly the ACE-positive and FCH negative lymph found to be positive in a second FCH PET/CT scan which was undertaken a few months later. Buchegger et al. [30] concluded that on the whole, ACE and FCH PET/CT scans did exhibit excellent concordance, on both a per-lesion, and per patient basis which would indicate that both tracers had performed equally for recurrent prostate cancer staging.

Castellucci et al. [31] undertook a study to assess the factors that could influence (11) C-choline PET/CT scan detection rate within a population of recurrent carcinoma of prostate gland patients who had been listed for salvage radiotherapy in an early phase of biochemical relapse, in order to select which of the patients could benefit most by the performance of re-staging (11) C-choline PET/CT scan prior to having salvage radiotherapy. Castellucci et al. [31] included in their study 605 patients who had undergone radical prostatectomy with curative intent for carcinoma of the prostate who had developed rising serum PSA levels pursuant to their primary therapy and had been listed for salvage radiotherapy. The patients' serum prostate-specific-antigen (PSA) levels were greater than 0.2 ng / m L, and less than ng / m L (mean, 1.1.05 ng / mL, median, 1.07 ng / m L, range 0.2 to 2.0 ng / m L, standard deviation, ± 0.59). All the patients had been classified as not having nodal disease (N0) after their radical prostatectomy. Seventeen of the 605 patients had adjuvant radiotherapy together with radical prostatectomy; on the other hand 148 of the patients had androgen deprivation therapy at the time of having their PET/CT scans. In order to assess which factor could influence PET/CT scan positivity, and the detection of local versus distant metastasis, the serum PSA levels, serum PSA kinetics, Gleason score, the ages of the patients, time to biochemical recurrence, androgen deprivation therapy, and the initial stage of the tumours, were analysed statistically. With regard to the results, Castellucci et al. [31] reported that (11) C-choline PET/CT was positive in 28.4% (positive in 172 out of the 605 patients). Eighty three out of the 605 patients had positivity within the pelvis (Group A), distant metastases were found in 72 out of the 605 patients (Group B), and local as well as distant sites of recurrence were found in 17 out of the 605 patients (Group C). The results of multivariate analyses did reveal that serum PSA level, serum PSA doubling time (PSAdt), and on-going androgen deprivation therapy (ADT) had constituted significant predictors for obtaining positive scan results; however, the serum PSA level, serum PSA doubling time (PSAdt) had been significantly related to the detection of distant recurrence ($P < 0.05$). Receiver-operating-characteristics analysis revealed that a serum PSA level of 1.05 ng / mL, and a serum PSA doubling (PSAdt) time of 5.95 months were the optimal cut-off values with regard to the prediction of a positive (11) C-choline PET/CT scan, with an area under the curve (AUC) of 0.625 for serum PSA and 0.677 for serum PSA doubling time (PSAdt). Castellucci et al. [31] made the following conclusions:

- (11) C-choline PET/CT scan may be suggested prior to salvage radiotherapy during the early phase of biochemical recurrence in order to select those patients who could benefit from this aggressive therapy.
- Especially, patients that show fast serum PSA kinetics or serum PSA increasing levels despite receiving androgen deprivation therapy (ADT) should undergo (11) C-choline PET/CT scan studies prior to undergoing salvage radiotherapy, taking into consideration that they tend to be associated with higher probability for the detection of positive findings outside the pelvis.

Poulsen et al. [32] compared the diagnostic accuracy of the ensuing imaging techniques with regard to the detection of spine metastases, with the use of magnetic resonance imaging (MRI) scan as a reference: whole body scintigraphy (WBS) with technetium-99m-MDP; [18F]-Sodium fluoride, [18F]-sodium fluoride (NaF) positron emission tomography (PET)/ computed tomography (CT) and [(18)F]-fluoromethylcholine (FCH) PET/CT. Poulsen et al. [32] stated that the entry criteria for their study included biopsy proven carcinoma of the prostate gland, a positive whole body scan (WBS) consistent with bone metastases, and no history of androgen deprivation therapy. Within 30 days of obtaining informed consent, the trial scans were undertaken in random fashion. The scans were interpreted blindly for the aim of a lesion-based analysis. The target variable for the study was bone lesion (malignant/benign). The gold standard was magnetic resonance imaging (MRI) scan findings. With regard to the results, Poulsen et al. [32] reported that they had enrolled 50 men with a mean age of 73 years, between May 2009 and March 2012. The median serum PSA level of the patients was 84 ng / m L, and the mean Gleason score of the tumours was 7.7. Forty six (46) of the patients had had all of the four scans, and 4 patients had missed one PET/CT scan. A total of 526 lesions were identified in the 50 patients and according to the MRI scan 353 of the lesions were benign and 163 of the lesions were not malignant. The sensitivity, specificity, positive and negative predictive values and accuracy of the study were recorded as: Whole body bone scan (WBS) – 51%, 82%, 86%, 43%, and 61% respectively; NAF-PET/CT scan – 93%, 54%, 82%, 78%, and 81% respectively; FCH PET/CT scan – 85%, 91%, 95%, 75%, and 87% respectively. Poulsen et al. [32] made the following conclusions:

- They had found that FCH PET/CT scan and NaF PET/CT scan were superior to WBS with regard to the detection of carcinoma of the prostate gland bone metastases within the spine.
- The results of their study would call into question the use of whole body scan (WBS) as the method of choice in patients with hormone-naïve carcinoma of the prostate gland.

Evangelista et al. [33] evaluated the efficiency of (18)F-Fluorocholine positron emission tomography /computed tomography (FCH PET/CT) in in the detection of lymph node and bone involvement in comparison with conventional imaging such as abdominal-pelvic CT scan and bone scan in the initial staging of carcinoma of the prostate gland. Evangelista et al. [33] evaluated 48 patients who had undergone FCH PET/CT scanning for the initial staging of carcinoma of the prostate gland. At the same time 32 out of the 48 patients had had a bone scan and 26 out of the 48 patients had also had CT scan of abdomen and pelvis. The diagnostic performance of the FCH PET/CT including the sensitivity, specificity, accuracy, was evaluated based upon patient basis for the entire population and also separately based upon risk-classification, and later in comparison with conventional imaging. Histological specimens or follow-up data had been used as the standard of reference. With regard to the results, Evangelista et al. [33] reported that the overall accuracy associated with FCH PET/CT

scan for lymph node involvement was 83.3%. The sensitivity of FCH was found to be higher in the case of the higher-risk subset of patients which was 83.3% than in the intermediate-risk group which was 33.3%, on the other hand, FCH specificity was similar compared with dedicated CT scan, FCH PET / CT scan was associated with a higher sensitivity and similar specificity (46.2%, versus 69.2%, 92.3% versus 92.3%) respectively. Additionally, the sensitivity and specificity of PET/CT scan were found to be higher than the sensitivity and specificity of bone scan (100% versus 90%, and 86.4% versus 77.2% respectively). As opposed to conventional imaging, PET/CT scan did change the staging of the carcinoma of the prostate gland in 33.3% of patients. Evangelista et a. [33] made the following conclusions:

- The efficiency of FCH PET/CT in the detection of both bone and lymph node involvement in carcinoma of the prostate gland at the initial staging was found to be higher in comparison with that of conventional imaging
- Prospective clinical trials would be required to confirm their findings.

Suardi et el. [34] had stated that traditionally patients who have been treated for adenocarcinoma of the prostate gland by means of radical prostatectomy who subsequently developed lymph node recurrence had tended to be managed by androgen deprivation approach. Suardi et al. [34] also said that even though there are no documented prospective studies, salvage lymph node dissection has been proposed as an alternative treatment option for lymph node recurrence pursuant to radical prostatectomy undertaken for localized carcinoma of the prostate gland. Suardi et al. [34] examined the long-term outcomes of salvage lymph node dissection who developed local lymph node recurrence diagnosed based upon 11C-choline positron emission tomography/computed tomography (PET/CT) scan. Suardi et al. [34] reported on 59 patients who had developed biochemical recurrence with 11C-choline with PET/CT scan showing pathologic activity who had undergone salvage lymph node dissection between 2002 and 2008. The patients did undergo pelvic and or retroperitoneal salvage pelvic lymph node dissection. With regard to outcome measurements and statistical analysis, Suardi et al. [34] defined biochemical response as serum prostate-specific antigen (PSA) level of < 0.2 at 40 days pursuant to the surgical operation of salvage lymph node dissection. Biochemical recurrence for those who achieved biochemical response was defined by Suardi et al. [34] as serum PSA level of > 0.2 ng / m L. Clinical recurrence was defined by Suardi et al. [34] as positive PET/CT scan pursuant to salvage lymph node dissection and in the presence of a rising serum PSA level. Kaplan-Meier curves were used to assess time to biochemical recurrence, clinical recurrence, and cancer-specific mortality. Cox regression had been fitted to assess the predictors of clinical recurrence. With regard to the results and limitations of the study, Suardi et al. [34] reported the following: The median follow-up of the patients was 81.1 months. On the whole, 35 patients (59.3%) did achieve biochemical response. The 8-year biochemical recurrence-free survival rate in patients who had achieved complete biochemical response was 23%. On the whole the 8-year clinical recurrence-free rate was 38% and the cancer-specific mortality-free rate was 81%. Suardi et al. [34] also reported that multivariable analyses were used to evaluate pre-operative variables and this showed that the serum PSA level at salvage lymph node dissection was the only predictor of clinical recurrence ($P = 0.03$). When post-operative parameters were taken into consideration, biochemical response and the presence of retroperitoneal lymph node metastases were found to be significantly associated with the risk of clinical recurrence ($P \leq 0.04$). Suardi et al. [34] were of the opinion that the limitation with regard to their study is the fact that there was no control group in the study for comparison. Suardi et al. [34] made the following conclusions.

- Salvage lymph node dissection could represent a therapeutic option in the treatment of patients who develop biochemical recurrence and nodal pathologic uptake at 11C-cholnie PET/CT scan pursuant to radical prostatectomy.
- Even though majority of the patients subsequently developed biochemical recurrence after salvage lymph node dissection, about 40% of the patients had experienced clinical recurrence-free survival.

Rowe et al. [35] reported a 45-year-old man who had presented 2 years prior to the time of having PET/CT imaging with elevated serum PSA level of 39 ng / m L and a suspected clinically localized carcinoma of the prostate gland. Histological examination of his trans-rectal ultrasound scan biopsy of his prostate gland showed features consistent with Gleason 5+4 = 9 adenocarcinoma of the prostate which had involved all biopsy cores. He had conventional imaging which did not reveal any evidence of metastasis. He underwent radical retro-pubic prostatectomy and during the operation there was evidence of extra-prostatic extension, seminal vesicle invasion, and positive bilateral pelvic lymph nodes. Pursuant to his prostatectomy his serum PSA level dropped to 10.5 ng / m L, and he later on received treatment by means of leuprolide and docetaxel which resulted in his serum PSA level dropping to 1.0 ng / m L. He was next enrolled series of clinical trials in which he received in succession, sipuleucel-T, anti-PDL1 therapy and enzalutamide with persistent elevation of his serum PSA up to 15.6 ng / m L, but the serum PSA level reduced to 1.0 ng / m L whilst he was receiving enzalutamide. At this point of his therapy he did have radiological imaging with whole body planar ^{99m} TC MDP bone scan, Na^{18}F PET/CT scan, and ^{18}F DCFPyL PET/CT scan. With regard to the results of the scans, Rowe et al. [35] reported that in all 89 lesions had been identified by at least one modality of scanning. Planar ^{99m}TC MDP bone scan did demonstrate 12 suspicious sites, Na^{18}F PET/CT scan did demonstrate 39 suspicious sites, and ^{18}F DCFPyL PET/CT scan did demonstrate 87 suspicious sites, of abnormal radiotracer uptake within the bones. Rowe et al. [35] stated with the assumption of all the 89 suspicious lesions being positive would yield a sensitivity of 13.5% for bone scan, 43.8% for the Na^{18}F PET/CT scan, and 97.7% for the ^{18}F DCFPyL PET/CT scan. Lesions that had been occult for planar ^{99m}TC MDP bone scan, and Na^{18}F PET/CT scan but had been apparent by ^{18}F DCFPyL PET/CT scan did include lesions that were entirely within the marrow cavity of the affected bone as well as in subtle sites abnormal cortical based uptake. Rowe et al. [35] stated that traditionally, imaging of bone metastases in carcinoma of the prostate gland had involved planar ^{99m}TC-methylene diphosphate (^{99m}TC MDP) bone scan with or without the use of supplemental tomographic imaging. However, over recent times, Na18 F positron emission tomography / X-ray computed tomography (PET/CT) scan had been found to have led to an improvement in the sensitivity and specificity for sites of osseous metastatic involvement. Roe et al. [35] further stated the following:

- Prostate-specific membrane antigen (PSMA) is a cell surface enzyme which would be highly useful in the assessment of carcinoma of the prostate gland and it had been explored as a target for the imaging of carcinoma of the prostate gland.
- PSMA-targeted PET/CT scan could offer improved sensitivity by binding directly to tumour cells, as opposed to localizing to sites of bony reaction.
- Their preliminary anecdotal finding should be explored in larger studies.

Agarwal et al. [36] reported a 55-year-old man who had metastatic Gleason 5+4 = 9 adenocarcinoma of the prostate gland for which he was undergoing Docetaxel chemotherapy. He was noted to have rising serum PSA levels and his serum PSA was recorded as 340 ng / m L and for this reason he had an isotope bone scan which did show diffusely increased skeletal accumulation with increased bone to soft tissue (renal uptake)

ratio which was suggestive of a metastatic super-scan. He additionally had gallium-68-prostate-specific membrane antigen 68 ((^{68}GaPSMA) PET/CT scan in order to evaluate him for ^{177}Lu-PSMA therapy. His maximum intensity projection image did show generalized increased tracer uptake in the entire axial as well as appendicular skeleton and reduced physiological uptake in bilateral lacrimal and salivary glands, spleen, small intestine, and kidneys. The sagittal and trans-axial positron emission tomography / computed tomography (PET/CT) scan fusion images did illustrate sclerotic changes in the whole axial skeleton with increased tracer uptake. Agarwal et al. [36] stated that all the aforementioned features were suggestive of metastatic super-scan on (^{68}GaPSMA) PET/CT scan. Based upon this case report it would be argued that PET/CT scan has the capability of demonstrating super-scan from disseminated adenocarcinoma of the prostate gland.

Su et al. [37] reported a 54-year-old man who had undergone radical prostatectomy and hormonal therapy for adenocarcinoma of the prostate gland. At his 7-years follow-up his serum PSA was noted to be elevated and he had magnetic resonance imaging scan as well as isotope bone scan which did not reveal any metastasis. He underwent radiotherapy under the presumption that he had local recurrence to no avail. One more year later he had F-FDG PET/CT scan which did show 3 FDG-avid lesions in the right lung and mediastinum. He underwent video-assisted thoracoscopic surgery and pathological examination of the excised lesions confirmed lung and lymph node metastases of adenocarcinoma of the prostate gland and at that time he also had bone scan which remained negative. The finding from this report would indicate that at times magnetic resonance imaging scan and isotope bone scan may not detect cases of early metastases of carcinoma of the prostate gland but F-FDG PET/CT scan could identify such recurrences that magnetic resonance imaging scan and bone scan are not able to detect.

Tong et al. [38] stated that carcinoma of the prostate gland constitutes a major health problem, and that routine radiological imaging does show only modest results in the detection and in the re-staging of localized carcinoma of prostate recurrence. Tong et al. [38] also stated that reports from studies undertaken recently had indicated promise of radiolabelled analogues of choline for positron emission tomography (PET) scans in patients who have biochemical recurrence and that sequentially incremental Fluorocholine (FCH) uptake tends to be associated with malignancy and that on the other hand decreasing tracer activity would tend to indicate benign aetiology; nevertheless, the aforementioned pattern of tracer activity had not been fully validated and no standardized (18)F-Fluorocholine ((18)F-FCH) has so far been put in place, Tong et al. [38] undertook a study in order to better define the role of dual-phase (18)F-FCH PET/computed tomography (CT) imaging with the use of retrospective masked reading focussing on the detection of loco-regional recurrence/metastasis in patients who had biochemical recurrence of disease pursuant to definitive local primary treatment of the tumour. Tong et al. [38] enrolled a total of 32 subjects between April 2010 and May 2014 who had histologically proven carcinoma of the prostate gland and who did undergo primary treatment of curative intent and who subsequently developed biochemical recurrence of disease. The early scans and delayed images of the pelvis were graded separately by blinded readers. The final evaluation was undertaken by using a combination of information obtained from dual-phase studies as “summative scan”. The maximum standardized uptake value was computed by using regions of interest that had been constructed over areas of focal hyperactivity. The calculations were undertaken by using Statistical Product and Service Solutions Version 20 for Windows. A composite reference which had consisted of histopathology, correlation with other imaging, or serum prostate-specific antigen (PSA) trend with clinical follow-up of at least 6 months was utilised to determine the true disease status of the patient. With regard to the results, Tong et al. [38] reported that early phase pelvis phase imaging sensitivity and specificity were computed to be 73.1% and 90.9% respectively and the late-phase pelvis imaging sensitivity and specificity were computed to be 80.8% and 100% respectively. The summation scan sensitivity and specificity were computed to be 76.9% and 100% respectively. The odds ratio of developing recurrent disease with an uptrend of SUV-max on dual-phase imaging was computed to be 33.3%. The optimal cut-off value of serum PSA was computed to be 1.85 ng / m L with 80% sensitivity and 62.5% specificity. Tong et al. [38] made the ensuing conclusions:

- Single-phase FCH PET/CT imaging is a reliable scanning modality which is capable of detecting sites of disease at low levels of serum PSA which still fulfil the criteria of biochemical recurrence.
- This would enable clinicians to identify sites which should be considered for potential biopsy or sites to be considered for loco-regional treatment.

Apolo et al. [39] undertook a prospective study which evaluated the capability of Na(18)F PET/CT scan to detect as well as monitor bone metastases over time including its correlation with clinical outcomes and survival in advanced carcinoma of the prostate gland. Apolo et al. [39] reported that sixty patients had carcinoma of the prostate gland including 30 patients who had confirmed bone metastases and 30 patients who did not have any bone metastases based upon conventional imaging, who had undergone Na(18)F PET/CT scan at baseline, at 6-months and at 12-months follow-up. Positive lesions had been verified on subsequent follow-up scans. Changes in SUVs and the number of lesion number(s) were correlated with the serum prostate-specific antigen (PSA) change, clinical impression and the overall survival. With regard to the results, Apolo et al. [39] reported that they did find significant associations which included the ensuing: SUV and prostate-specific antigen (PSA) percentage change at 6 months ($P = 0.014$) and 12 months ($P = 0.005$); SUV maximal percentage change from base-line and clinical impression at 6 months ($P = 0.0147$), and 6 to 12 months ($P = 0.053$); SUV change at 6 months and overall survival ($P = 0.018$); number of lesions on Na(18)F PET/CT scan and clinical impression at base-line ($P < 0.0001$), 6 months ($P = 0..0078$), and at 12 months ($P = 0.0029$); and number of lesions on Na(18)F PET/CT per patient at base-line and overall survival ($P = 0.017$). Apolo et al. [39] stated that with regard to paired-exploratory analysis, paired (99m) Tc-methylene diphosphonate bone scans ((99m)Tc-BS were available for 35 patients at base-line, 19 patients at 6 months, and 14 patients at 12 months (68 scans). Malignant lesions on Na(18)F PET/CT scans (total number 57) were classified on (99m) Tc-BS as malignant 65% of the time, indeterminate 25% of time, and negative 10% of the time. Furthermore, 69% of paired scans did show more lesions on Na(18)F PET/CT scans in comparison with on (99m) Tc-BS. Apolo et al. [39] made the ensuing conclusions:

- The base-line number of malignant lesions and changes in SUV on follow-up Na (18) F PET/CT scans did significantly correlate with clinical impression and overall survival.
- Na (18) F PET/CT scans, tend to detect more bone metastases earlier in comparison with (99m) Tc-BS and tends to enhance the detection of new bone disease in high-risk patients.

Lavalaye et al. [40] reported a 75-year-old man who was diagnosed as having Gleason 9 adenocarcinoma of the prostate gland. His serum prostate-specific antigen (PSA) was noted to be 5.04 ng / m L. He had a routine isotope bone scan which was negative in that it did not show any evidence of bone metastasis. (a) In view of the high histological grading of his tumour and the relatively high level of his serum PSA, (68)Ga-PSMA PET/CT scan was requested in order to confirm or exclude distant metastasis. The (68)Ga-PSMA PET/CT scan did show several skeletal lesions which had high tracer accumulation as a sign of diffuse bone metastases. (b) On low-dose CT scan there was no evidence of sclerosis.

(c) The (68)Ga-PMSA PET/CT scan also did show high uptake in the prostate gland, and in the para-aortic lymph nodes, as well as in the para-iliac lymph nodes, without any evidence of any lymph node enlargement. Lavalaye et al. [40] stated that unfortunately biopsy of the bone was not undertaken in order to confirm histologically presence of metastases from carcinoma of the prostate gland. In view of the PET/CT scan findings the patient's treatment plan was changed to systemic therapy rather than the local therapy which was originally planned. It would be argued from the findings of this case report that in some cases of bone metastasis in the early stage of bone metastasis from carcinoma of the prostate gland (68)Ga-PSMA PET/CT scan could show evidence of bone metastasis which isotope bone scan may not be able to pick despite the fact that bone biopsy was not undertaken to prove for certainty that the metastases were from adenocarcinoma of the prostate gland.

Graziani et al. [41] evaluated the use of (11)C-choline PET/CT scan as a diagnostic tool for the re-staging of carcinoma of the prostate gland in a large homogeneous and clinically relevant population of patients who had biochemical recurrence of carcinoma of the prostate gland pursuant to undergoing primary treatment for carcinoma of the prostate gland. Graziani et al. [41] also assessed the best timing for the performance of (11) C-choline PET/CT scan during the period of biochemical recurrence. Graziani et al. [41] retrospectively analysed 9,632 (11)C-choline PET/CT scans which had been performed in their institution for the re-staging carcinoma of the prostate gland from January 2007 to June 2015. The inclusion criteria for the study were: (1) Proven case of carcinoma of the prostate gland which had been treated by means of radical prostatectomy or by means of external beam radiotherapy; (2) Serum prostate-specific antigen (PSA) level results of the patient must be available; (3) There must be evidence of proven biochemical recurrence (BCR) (PSA > 0.2 ng / mL pursuant to radical prostatectomy or serum PSA > 2.0 ng / mL above the nadir pursuant to primary external beam radiotherapy with rising serum PSA levels). In the end 3,203 patients who had recurrent carcinoma of the prostate gland that matched the study inclusion criteria had been retrospectively enrolled into the study and all together 4,426 scans were analysed. With regard to the results, Graziani et al. [41] reported that on the whole 52.8% of the (11) Choline PET/CT scan (2,337/4,426) and 54.8% of the patients (1,755/3203) were positive. With regard to 29.4% of the scans, at least one distant metastasis (positive lesion) was identified. The median and mean serum PSA levels were respectively recorded as 4.9 ng / mL and 2.1 ng / mL at the time of the PET/CT scan and the serum PSA levels had ranged between 02 ng / mL and 50.0 ng / m L. Graziani et al. [41] also reported that in their study, 995 PET/CT scans had been performed in patients whose serum PSA levels had ranged between 1 ng / mL and 2 ng / m L. Graziani et al. [41] further reported the following:

- In their subpopulation of patients studied, the positivity rate of the 995 PET/CT scans was 44.7%, with a documented incidence of distant findings in 19.% of patients, as well as an incidence of oligometastatic disease (one to three lesions) in 37.7% of cases.
- The absolute value of the serum PSA at the time of the PET/CT scan and the on-going androgen deprivation therapy had been associated with an increased probability of a positive (11) Choline PET/CT scan result ($p < 0.001$).
- The ROC analysis did reveal that a serum PSA value of 1.16 ng / m L had been the optimal cut-off value.
- With regard to patients who had serum PSA value less than 1.16 ng / m L, 26.8% of 1,426 (11) choline PET/CT had been positive with oligometastatic disease in 84.7% of the positive scans.

Graziani et al. [41] made the ensuing conclusions:

- The results of their study of a large cohort of patients had confirmed the feasibility of (11) Choline PET/CT scan for the detection of sites of metastatic disease in patients with carcinoma of the prostate gland who had developed biochemical recurrence
- The serum PSA level had been identified as the main predictor of a positive (11) choline PET/CT positive scan with 1.16 ng / m L as the optimal cut-off value.
- In the majority of positive (11) Choline PET/CT scans oligometastatic disease which is potentially treatable by salvage therapies had been observed.

Paone et al. [42] reported the incidental detection of Hurtle cell adenoma by using 18—choline PET/CT scan in a patient with prostate cancer which would although be anecdotal, would indicate that 18-cholne PET/CT scan has the capability of detecting malignant lesions as well as non-malignant lesions at times hence histological examination would be required to confirm a definite diagnosis of lesions that are picked up by this form of PET/CT scan; however, with regard to adenocarcinoma of prostate gland which had been originally treated by means of radical radiotherapy, a CT scan undertaken in the planning of the radiotherapy would have picked up the lesion earlier, therefore in the follow-up PET/CT scanning in the case of biochemical failure the problem of finding a de novo benign lesion would be avoided. The article published by Paone et el. [42] was published in Spanish and the details are not available to the author.

Oprea-Lager et al. [43] reported 12 patients (mean age ± SD; 64 years ± 8 years) who had metastasized carcinoma of the prostate gland who had undergone two sets of (18)F-fluoromethylcholine PET/CT scans, on consecutive days. Each seat of the PET/CT scan did consist of a thirty minutes dynamic PET/CT scan of the thorax pursuant to intravenous administration of 200 MBq of (18)F-fluoromethylcholine, which was ensued by a whole body PET/CT scan at 40 minutes. The dynamic scan was utilized to derive the area under the blood activity concentration curve. The lesion uptake was derived from the whole body PET/CT scan by using a variety of types of volumes of interest: maximum, peak, and mean. Each of the aforementioned parameters was normalized to injected activity per body weight, area under the blood activity concentration curve, and blood concentration itself at 40 minutes, which did result in a number of types of SUVs including: SUV, SUVAUC, and SUVTBR. The test-retest repeatability of the aforementioned metrics and the metabolic tumour volume (MTV), as well as total uptake of choline within the lesion, had been studied. The level of agreement between the test-retest data and reliability was evaluated by using Bland-Altman plots, repeatability coefficients, and intra-class correlation coefficients (ICCs). With regard to the results, Oprea-Lager et al. [43] reported that they had identified a total of 67 choline-avid metastatic lesions which included 44 bone lesions, and 23 lymph node lesions. With regard to the SUVmax, the repeatability coefficient for SUV, SUVAUC, and SUVTBR were recorded as 26% (ICC, 0.95), 31% (ICC 0.95), and 46% (ICC 0.89), respectively. Oprea-Lager et al. [43] also reported that they had obtained similar values for SUVpeak, and SUVmean and furthermore, the repeatability of SUVAUC had been comparable to that of SUVmax, SUVpeak, as well as SUVmean. Oprea-Lager et al. [43] additionally found that the tissue type and localization of the tumour did not in any way affect the repeatability. Oprea-Lager et al. [43] made the ensuing additional findings: An MTV of less than 4.2 cubic centimetres did have larger variability in comparison with larger volumes (with repeatability coefficient of 45%, versus 29%; P=0.048). The repeatability coefficient was found not to be significantly different between lesion that had SUVpeak above or below the median value of 8.3 (19% versus 28%; P = 0.264). Oprea-Lager et al. [43] made the following conclusions: The repeatability of SUVAUC had been comparable with that of standard SUV. The repeatability of a variety of semi-quantitative (18)F-fluoro-methyl-choline parameters (SUV, MTV, and total uptake within the lesion) had been about 35%. Larger differences could likely be related to

treatment effects. The findings of Oprea-Lager et al. [43] would indicate the repeatability of quantitative 18F-Fluromethylcholine PET/CT scan studies in carcinoma of the prostate gland as well as its potential of being used to localize or detect metastatic carcinoma of prostate in the nodes as well as distant sites .

Morris et al. [44] made the following iterations: (a)The current FDA-approved radiology imaging modalities are not adequate for the localization of prostate cancer biochemical recurrence (BCR). (b) ^{18}F-DCFPyL is a highly selective, small-molecule prostate-specific membrane antigen-targeted PET radiotracer. (c) CONDOR represented a prospective designed study to ascertain the performance of ^{18}F-DCFPyL-PET/CT scan in patients who had biochemical recurrence (BCR) of prostate cancer and uninformative standard radiology imaging. With regard to the experimental design of the CONDOR phase III, Multi-centre study, Morris et al. [44] stated that men who had rising serum PSA that was equal to or greater than 0.2 ng/mL pursuant to prostatectomy or equal to or higher than 2 ng/mL above nadir pursuant to undergoing radiotherapy were eligible for the study. The primary end point of the study was the correct localization rate (CLR), which was defined as positive predictive value with an additional requirement of anatomic lesion localization between ^{18}F-DCFPyL-PET/CT scan and a composite standard of truth (SOT). The SOT did consist of, in descending priority: (i) histopathology, (ii) subsequent correlative imaging findings, or (iii) post-radiotherapy serum PSA response. The trial was regarded as successful if the lower bound of 95% confidence interval (CI) for CLR had exceeded 20% for two out of three ^{18}F-DCFPyL-PET/CT scan readers. The secondary end points of the study did include change with regard to the intended management and safety. With regard to the results, Morris et al. [44] reported the following: (a) A total of 208 men whose baseline serum prostate specific antigen (PSA) had ranged between 0.2 ng/mL and 98.4 ng/mL, and whose median baseline serum PSA was 0.8 ng/mL did undergo ^{18}F-DCFPyL-PET/CT scanning. (b) The CLR was noted to be 84.8% to 87.0% (lower bound of 95% CI: 77.8-80.4). In view of the results of the ^{18}F-DCFPyL-PET/CT scan, a total of 63.9% of the evaluable patients did have a change in their intended management. (d) The detection rate of the disease was 59% to 66% in that at least one lesion was identified per patient by ^{18}F-DCFPyL-PET/CT scan by central readers. Morris et al. [44] made the following conclusions: (a) The undertaking of ^{18}F-DCFPyL-PET/CT scan had achieved the primary end point of the study by demonstrating the localization of the disease in the setting of negative standard radiology imaging and by providing information that was clinically meaningful as well as actionable. (b) These data additionally supported the undertaking of ^{18}F-DCFPyL-PET/CT scan to localize disease in men who had recurrent carcinoma of the prostate gland.

Roberts et al. [45] stated that Prostate-specific membrane antigen (PSMA) positron emission tomography (PSMA-PET) scan does improve the staging of carcinoma of the prostate gland. They also stated that intra-prostatic PSMA intensity could predict clinically relevant oncological outcomes of prostate cancer. Roberts et al. [45] undertook a study that was aimed to investigate the relationship between intra-prostatic PSMA intensity and adverse outcomes of pathology, with the inclusion of biochemical progression-free survival (PFS) pursuant to radical prostatectomy. Roberts et al. [] reported that their study included a cohort study of 71 patients who had MRI-guided, biopsy-proven carcinoma of prostate gland as well as pre-operative 68Ga-PSMA-11 PET/CT scan preceding their undergoing radical prostatectomy (RP). Roberts et al. [45] correlated intra-prostatic PSMA intensity to adverse pathology outcomes (Gleason score and upgrading from biopsy, pathology stage as well as PFS with utilization of multi-variate statistical analysis. Roberts et al. summarized the results as follows:

- ^{68}Ga-PSMA-11 PET/CT intensity in vivo did predict all of Gleason score on radical prostatectomy, up-grading from biopsy to radical prostatectomy (RP) histopathology, pathology stage, positive surgical margins and progress-free survival (PFS) 74.6% (53 out of 71) of the patients were free from progression at a median follow-up of 19.5 months and which had ranged between 0.4 months to 48 months.
- The predictive accuracy was noted to be particularly enhanced by PSMA among patients who had pathology examination of biopsy showing Gleason score less than or equal to 3+4 in 39 patients which represented the most significant predictor of progress free survival (PFS) according to Cox-proportional hazards regression.
- Cox-regression adjusted survival analysis did predict a 5.48-fold increase in hazard for Gleason $\leq 3+4$ patients who had high (SUVmax >8) in comparison with low (SUVmax <8) PSMA intensity.

Roberts et al. [45] concluded that intra-prostatic ^{68}Ga-PSMA-11 intensity is prognostic and it could be a valuable new biomarker with regard to localized carcinoma of the prostate gland, especially with regard to men who have biopsy proven Gleason 3+4 = 7 disease considering an initial approach of active surveillance or focal treatment.

Fanti et al. [46] iterated that prostate-specific membrane antigen (PSMA) positron emission tomography (PET) / computed tomography (CT) scan is utilized for re-staging prostate cancer (PCa) as well as it is utilized as a biomarker for the evaluation of response to treatment; nevertheless, prostate-specific membrane antigen (PSMA) positron emission tomography (PET) / computed tomography (CT) scan does lack established response criteria. In view of this a panel of prostate cancer (PCa) experts in nuclear medicine, radiology, and / or Urology met on the 21st of February 2020, in Amsterdam, The Netherlands, in order to formulate criteria for PSMA – PET/CT based response in patients who undergo treatment for metastatic carcinoma of the prostate (PCa) as well as the optimal timing for the utilization of prostate-specific membrane antigen (PSMA) positron emission tomography (PET) / computed tomography (CT) scan. With regard to the methods, Fanti et al. [46] stated that the panel members had received thematic topics as well as relevant literature preceding their meeting. They developed statements on how to interpret response and progression on treatment in prostate cancer (PCa) with prostate-specific membrane antigen (PSMA) positron emission tomography (PET) / computed tomography (CT) scan, as well as when to use prostate-specific membrane antigen (PSMA) positron emission tomography (PET) / computed tomography (CT) scan. The panel members voted anonymously on a nine-point scale that ranged from strongly disagree (1) to strongly agree (9). The median scores did describe agreement as well as consensus opinion. Fanti et al. [46] summarised the results as follows (see table 1):

- Prostate-specific membrane antigen (PSMA) positron emission tomography (PET) / computed tomography (CT) scan consensus statements did concern utility, best timing for the undertaking of the scan, the criteria for the evaluation of response, patients who could benefit from prostate-specific membrane antigen (PSMA) positron emission tomography (PET) / computed tomography (CT) scan, and handling of radio-labelled PSMA PET tracers.
- Consensus was reached on all statements.
- Prostate-specific membrane antigen (PSMA) positron emission tomography (PET) / computed tomography (CT) scan, can be utilized before as well as after local and systemic treatment in patients who have metastatic disease in order to evaluate response to treatment.

- Ideally, prostate-specific membrane antigen (PSMA) positron emission tomography (PET) / computed tomography (CT) imaging scan criteria should categorize the patients as responders, patients who have stable disease, partial response, and complete response, or as non-responders.
- Specific clinical scenarios such as oligometastatic or poly-metastatic disease deserve special consideration.

Fanti et al. [46] made the ensuing conclusions:

- Adoption of prostate-specific membrane antigen (PSMA) positron emission tomography (PET) / computed tomography (CT) scan should be supported by indication for appropriate utilization as well as precise criteria for interpretation.
- Prostate-specific membrane antigen (PSMA) positron emission tomography (PET) / computed tomography (CT) scan criteria should categorize patients as responders or non-responders.
- Specific clinical scenarios do deserve special consideration.

Thematic topic and corresponding statement				
Statement		MAS	IPR	IPRAS
1. Can PSMA PET/CT be used before and after any treatment?				
1.1	In principal, PSMA PET/CT can be used before and after any local and systemic treatment in patients at risk of having metastatic disease (including N1 disease).	8	1	7.6
1.2	PSMA PET/CT should not be used if no change of clinical management is expected.	9	0	8.35
1.3	PSMA PET/CT should not be used if local disease within the prostate is expected.	8	1	7.6
1.4	After salvage treatment of oligometastatic PCa with curative intent, if PSA indicates complete response, PSMA PET/CT is to be avoided as an assessment tool.	9	0.6	7.9
1.5	Routine use of PSMA PET/CT should not be used in patients with hormone sensitive PCa and PSA response under systemic therapy.	8	0.6	7.3
1.6	Routine use of PSMA PET/CT should not be used in patients with late-stage disease where no further therapies can be initiated.	7	0	5.35
2. What is the best timing for performing PSMA PET/CT?				
2.1	In cases where the primary PCa is negative on PSMA PET/CT, further staging with PSMA PET/CT is generally not adequate, and other imaging should be performed.	9	0	8.35
2.2	If used for response assessment, then a PSMA PET/CT should be performed before the start of treatment (i.e., baseline PSMA PET/CT).	9	0	8.35
2.3	PSMA PET/CT should not be performed within three months after initiation of systemic therapy in hormone sensitive PCa.	9	1	7.6
2.4	PSMA PET/CT should not be performed for routine follow-up if management of the patient is unlikely to change.	9	0.6	7.9
3. Which PET criteria should be used to evaluate the PSMA response?				
3.1	For clinicians, PSMA PET/CT should always be accompanied by evaluation of clinical and laboratory data.	9	0	8.35
3.2	For imaging specialists, only treatment response criteria for PSMA PET/CT are needed (not taking other parameters into account (e.g. PSA, etc.).	9	1	7.6
3.3	Ideally, PSMA PET/CT criteria should categorize patients as responders or non-responders.	9	0	8.35
3.4	Categories of responders should include patients with stable disease and partial and complete response on PSMA PET/CT imaging; non-responders should include patients with progressive disease on PSMA PET/CT.	8	1.2	6.85
3.5	In early recurrent PCa, appearance of any new lesion with high suspicion should be regarded as progressive disease.	8	1	7.6
3.6	In polymetastatic PCa, increase of uptake or tumour volume > 30% is defined as progressive disease.	8	1	7.6
3.7	In polymetastatic PCa, appearance of two or more new lesions should not be regarded as progressive disease, if total tumour volume or uptake does not increase > 30%.	9	1	7.6
3.8	PCWG3-criteria for evaluation of bone scintigraphy should not necessarily be used for PSMA PET/CT evaluation.	9	0.6	7.9
3.9	Complete response: complete disappearance of any lesion with tracer uptake; partial response: reduction of uptake and tumour volume by > 30%; SD: change of uptake and tumour volume ± ≤ 30% and no new lesions; progressive disease: appearance of two or more new lesions and/or increase of uptake or tumour PET volume > 30%.	9	0.6	7.3
4. Which patients could benefit from PSMA response assessment from a clinical perspective (other than those for whom a treatment change will have a significant impact on outcome)?				
4.1	PSMA PET/CT response assessment should be evaluated in the context of clinical trials.	9	0	8.35
4.2	In clinical practice, PSMA PET/CT response assessment may be performed in patients with inconsistent laboratory findings and/or clinical course of the disease if change of management is considered.	9	0	8.35
5. How should the various PET tracers be handled?				

5.1	Different ^{68}Ga and ^{18}F radiolabelled PSMA tracers (e.g., [^{68}Ga]Ga-PSMA-11, [^{18}F]PSMA-1007, and [^{18}F]DCFPyL) show similar performance even if there is lack of comparative data.	8	1	7.6
5.2	For response assessment the same PSMA PET tracers should be used.	9	0	8.35
5.3	Quality assurance is mandatory either for radiotracer production and image acquisition and should include EARL-harmonized protocols (scanner, reconstruction algorithms) regarding dosage, time of acquisition and quantification should be done using validated software.	9	0	8.35
6. Other relevant statements				
6.1	Available real-world data and/or trial data should be analysed for response assessment with PSMA PET/CT before designing future prospective trials.	9	0	8.35
6.2	Criteria for treatment assessment should be evaluated in test-retest trials to assess normal variability in the measurement.	9	1	7.6

Abbreviation: EARL, European Association of Nuclear Medicine Research Ltd.; IPR, inter-percentile range; IPRAS, inter-percentile range adjusted for symmetry; MAS, median agreement score; PCa, prostate cancer

Table 1: Consensus statements on PSMA PET/CT response assessment criteria along with their respective median agreement scores (MAS), inter-percentile ranges (IPR), and inter-percentile ranges adjusted for symmetry (IPRAS)

From: Consensus statements on PSMA PET/CT response assessment criteria in prostate cancer

Table 1: Reproduced from: Fanti, S., Goffin, K., Hadaschik, B.A. et al. Consensus statements on PSMA PET/CT response assessment criteria in prostate cancer. Eur J Nucl Med Mol Imaging **48,** 469–476 (2021). https://doi.org/10.1007/s00259-020-04934-4 https://link.springer.com/article/10.1007/s00259-020-04934-4#citeas https://link.springer.com/article/10.1007/s00259-020-04934-4/tables/1

Jansen et al. [47] stated that the detection of lymph-node metastases (N1) with utilization of conventional radiology imaging such as magnetic resonance imaging (MRI) and computed tomography (CT) scan is not adequate for primarily diagnosed prostate cancer (PCa). They also iterated that prostate-specific membrane antigen (PSMA) positron emission tomography (PET) / computed tomography (CT) scan has been successfully introduced for the staging of biochemically-recurrent prostate cancer (PCa). They additionally stated that apart from the frequently utilized 68gallium-labelled PSMA tracers, 18fluorine-labelled PSMA tracers are available. Jansen et al. [47] undertook a study which did examine the diagnostic accuracy of 18F-DCFPyL (PSMA) PET/CT for lymph-node staging in primary prostate cancer (PCa). With regard to the methods, Jansen et al. [47] stated the following: Their study was a prospective, and multi-centre cohort study. Patients who had primary prostate cancer (PCa), did undergo 18F-DCFPyL PET/CT scan preceding their undergoing robot-assisted radical prostatectomy (RARP) with extended pelvic lymph-node dissection (ePLND). The patients were included from the period of time between October 2017 and January 2020. A Memorial Sloan Kettering Cancer Centre (MSKCC) nomogram risk probability of $\geq 8\%$ of lymph-node metastases was set to undertake ePLND. All the radiology images were reviewed by two very experienced nuclear physicians and the images were compared with the post-operative histopathology examination findings of the surgical specimens. Jansen et al. [47] summarized the results as follows:

- A total of 117 patients were analysed.
- Lymph-node metastases (N1) were diagnosed based upon histopathology examination of the specimens in 17 out of 117 patients which amounted to 14.5% of the patients.
- The sensitivity, specificity, positive predictive value and negative predictive value for the 18F-DCFPyL PET/CT detection of pelvic lymph node metastases on a patient level were 41.2% (confidence interval (CI): 19.4 – 66.5%), 94.0% (CI 86.9 – 97.5%), 53.8% (CI 26.1 – 79.6%), and 90.4% (CI 82.6 – 95.0%), respectively.

Jansen et al. [47] made the ensuing conclusions:

- 18F-DCFPyL PET/CT scan did show a high specificity (94.4%), yet a limited sensitivity (41.2%) for the identification of pelvic lymph-node metastases in primary prostate cancer (PCa).
- This does imply that current PSMA PET/CT radiology imaging scan cannot replace diagnostic extended pelvic lymph node dissection (ePLND).
- Subsequent additional research would be necessary in order to define the exact place of PSMA PET? CT radiology imaging in the staging of primary prostate cancer (PCa).

Afshar-Oromieh, et al. [48] evaluated the performance of [^{68}Ga] Ga-PSMA-11 PET/CT scan with regard to the diagnosis of recurrent prostate cancer (PC) pursuant to prostatectomy in a large multi-centre cohort of patients. With regard to the methods of their study, Afshar-Oromieh, et al. [48] stated the following: The centres which had contributed to their study, were departments of nuclear medicine of Heidelberg in Germany, Technical University of Munich in Germany, and Albert Einstein Hospital of São Paulo in Brazil. A total of 2533 individual patients who had been scanned with the undertaking of [^{68}Ga] Ga-PSMA-11 PET/CT at 1 h p.i. due to recurrent PC pursuant to their undergoing prostatectomy were included in their retrospective analysis. Afshar-Oromieh, et al. [48] stated that their exclusion criteria included the following: Patients who had untreated primary tumour; previous chemotherapy or Xofigo®; those patients who had been previously treated exclusively by means of external beam radiotherapy of by means of HIFU; those who had been referred for PSMA-treatment; as well as those individuals who had undergone treatment with ADT including first- and second generation ADT within the preceding 6 months. They evaluated in a multivariable analysis potential influences of different factors including: serum PSA level, Serum PSA doubling time (PSADT), Serum PSA velocity (PSAvel), Gleason Score (GSC, with the inclusion of the separate 7a and 7b), age

and amount of injected tracer. Afshar-Oromieh, et al. [48] reported the results as follows:

- The rate of pathologic PET/CT-scans was 43% for serum PSA that was equal to or less than 0.2 ng/mL, 58% for serum PSA that was higher than 0.2 up to equal to or less than 0.5 ng /mL, 72% for serum PSA that was greater than 0.5 ng /mL to equal to or less than 1.0 ng / mL, and this increased to a maximum of 93% for serum PSA higher than 10 ng / mL
- A pathological PET/CT scan finding was noted to be significantly ($p = 0.001$) associated with serum PSA level and higher GSC.
- The amount of injected tracer, the age of the patient, serum $PSA_{DT,}$ serum PSA_{Vel} were found not to be associated with a higher probability of a pathological scan.

Afshar-Oromieh, et al. [48] made the following conclusions:

- .[^{68}Ga]Ga-PSMA-11 PET/CT at 1 h p.i. did confirm its high performance in the largest patient cohort that had been analysed.
- The detection of tumour did demonstrate a clear association with higher serum PSA level as well as higher GSC.
- They did not find any association between a pathological [^{68}Ga] Ga-PSMA-11 PET/CT and age, amount of injected tracer, PSA_{DT} or PSA_{Vel}.

Baucknehet, et al. [49] undertook a study to ascertain whether the prognostic value of 18 F-Fluorodeoxyglucose Positron Emission Tomography / Computed Tomography (FDG-PET/CT) scan in metastatic castration-resistant prostate cancer (mCRPC) does extend to the estimation of systemic treatment response duration. Baucknehet, et al. [49] retrospectively enrolled mCRPC patients who had undergone FDG-PET/CT scan within four Italian centres from 2005 to 2020. Baucknehet, et al. [49] collected the clinical as well as biochemical data at the time of radiology imaging as well as they calculated the SUV max of the hottest lesion, the total metabolic tumour volume (MTV) as well as the total lesion glycolysis (TLG). Baucknehet, et al. [49] analysed the correlation between PET-CT scan as well as biochemical-derived parameters with the Overall Survival (OS). They also assessed the prediction of treatment response duration in the sub-group of patients who had undergone FDG-PET/CT scan within the six months preceding Chemotherapy that consisted of Docetaxel or Cabazitazel in 24 of the patients, or Androgen-Receptor Targeted Agents (ARTA, namely Abiraterone or Enzalutamide in 20 patients. Baucknehet, et al. [49] summarized the results as follows:

- They had enrolled 114 mCRPC patients who had been followed-up for a median interval that lasted 15 months.
- They found out that at univariate analysis, serum prostate-specific antigen (PSA), Alkaline Phosphatase (ALP), MTV, as well as TLG were associated with overall survival (OS), and at the multi-variate Cox regression analysis, the sole MTV could independently predict overall survival (OS) ($p < 0.0001$).
- Within the sub-group that had been submitted FDG-PET/CT scan preceding the initiation of systemic treatment, serum PSA and TLG could also predict the duration of treatment response independently. ($p < 0.05$).
- They had noted that, whilst serum PSA level could not indicate the best choice of treatment, lower TLG was found to be associated with higher success rates for ARTA but it did not have any impact upon the efficacy of chemotherapy.

Baucknehet, et al. [49] concluded that FDG-PET/CT scan's prognostic value does extend to the prediction of the duration of treatment response in mCRPC, thus it does potentially guide the selection of systemic treatment.

Klingenberg et al. [50] iterated that with the largest high-risk prostate cancer (PCa) cohort to date that had undergone ^{68}Ga-prostate-specific membrane antigen (PSMA) PET/CT primary staging, it was their aim to characterize the metastatic spread of prostate cancer (PCa) with regard to tumour ^{68}Ga-PSMA uptake and the D'Amico classification and secondly, to compare ^{68}Ga-PSMA PET/CT findings with radical prostatectomy and pelvic lymph node dissection (PLND) histopathology findings. With regard to the method of their study, the study had included 691 consecutive newly diagnosed, histopathology examination biopsy proven, treatment-naïve, D'Amico high-risk prostate cancer (PCa) patients who were primary-staged based upon ^{68}Ga-PSMA PET/CT scan. Klingenberg et al. [50] compared PSMA SUV_{max} and metastatic findings were with the serum prostate-specific antigen level, International Society of Urological Pathology (ISUP) grade of the tumour, and the clinical stage as traditional risk stratification parameters. Additionally, Klingenberg et al. [50] compared the ^{68}Ga-PSMA PET/CT findings with histopathology examination findings in radical prostatectomy patients who had undergone pelvic lymph node dissection (PLND). Undetected lymph node metastases (LNMs) were assessed based upon the undertaking of immunohistochemical staining for PSMA. Klingenberg et al. [50] summarized the results as follows:

- They had observed that advanced disease (N1/M1) in 35.3% of the patients which accounted for 244 patients out of 601 patients and this was found to be associated with increasing serum prostate-specific antigen level, ISUP grade, and clinical stage.
- They had detected LNMs (N1/M1a) were in 217 out of 691 patients that amounted to 31.4% and bone metastases (M1b) in 116 out of 691 patients that amounted to 16.8% of the patients.
- They also found that advanced disease frequencies in patients who had ISUP grades 2 and 3 were 11 out of 102 patients that amounted to 10.8% of the patients and 33 out of 89 patients that amounted to 37.1% of the patients.
- The risk for the development of advanced disease for cT2a, cT2b, and cT2c tumours was found to be almost equal which did amount to 24.2%, 27.9%, and 22.4%, respectively.
- They did observe a weak correlation between SUV_{max} and biopsy ISUP grade ($\rho = 0.21$; $P < 0.001$) as well as a modest correlation between SUV_{max} and post-prostatectomy ISUP grade ($\rho = 0.38$; $P < 0.001$).
- They had also found that the sensitivity, specificity, positive and negative predictive value, and accuracy for LNM detection based upon ^{68}Ga-PSMA PET/CT scan in the pelvic lymph node dissection (PLND) cohort of patients were 30.6%, 96.5%, 68.8%, 84.5%, and 83.1%, respectively.
- They also found that undetected LNMs were either micro-metastases that had been located within the lymph node border or they were without the expression of PSMA

Klingenberg et al. [50] made the ensuing conclusions:

- Within this high-risk prostate cancer (PCa) cohort of patients, they had identified advanced disease in approximately one third during the diagnosis.
- They had also observed that ISUP grade represented the superior predictor for advanced disease at the time of the diagnosis of the tumour.

- They did also find a significant difference with regard to the frequency of advanced disease between ISUP grades 2 and 3, which also supported the Gleason score 7 subdivision.
- They did not find any significant differences with regard to the risk for the development of advanced disease when they compared the different cT2 stages. The undetected LNMs were found to be either PSMA-negative or micro-metastases...

Satapathy et al. [51] iterated that an early diagnosis is pertinent with regard to the overall management of carcinoma of the prostate gland and that Gallium-68-labeled prostate-specific membrane antigen (PSMA) PET / CT scan does have an established role with regard to the detection of recurrent prostatic carcinoma disease and patients who have intermediate – to high-risk carcinoma of the prostate gland. Nevertheless, only a small number of studies had undertaken an evaluation of the role of PSMA PET/CT scan in the initial diagnosis of carcinoma of the prostate gland. Satapathy et al. [51] undertook a systematic review in order to ascertain the diagnostic performance of ^{68}Ga-PSMA PET/CT with regard to the initial detection of carcinoma of the prostate gland in patients who have clinical or biochemical blood test findings that are considered to be suspicious for the diagnosis of prostate cancer. In order to write their article Sapathaty et al. [51] searched for literature on PSMA PET/CT scan in prostate cancer for data bases that included PUBMED, Scopus, and Embase with utilization of relevant keywords for articles that had been published through 30th April 2020 which they had included. They utilized the histopathology examination results as the reference standard, the numbers of true- and false-positives as well as true- and false-negatives which they extracted. With utilization of bivariate random-effects meta-analysis, they generated pooled estimates of diagnostic test accuracy-including sensitivity, specificity, positive likelihood ratio, negative likelihood ration, as well as summary ROC (SROC) curve. They included seven studies that had comprised of 389 patients in the systematic review and meta-analysis. Sapathaty et al. [51] found the following:

- The pooled sensitivity, specificity, positive likelihood ratio, and the negative likelihood ratio for the initial diagnosis of prostate gland with utilization of ^{68}Ga-PSMA PET/CT scan were 0.97 (95% CI, 0.90-0.99), 0.66 (95% CI, 0.52-0.78), 2.86 (95% CI, 1.95-4.20), and 0.05 (CI, 0.01-0.15) respectively.
- The test was found to have high accuracy and the area under the SROC curve was 0.91 (95% CI, 0.88 – 0.93).

Sapathaty et al. [51] concluded that Gallium-68-labeled PSMA PET/CT scan had excellent sensitivity as well as negative likelihood ratio with regard to the initial diagnosis of carcinoma of the prostate gland in patients who have clinical or biochemical blood test findings that are considered to be suspicious for the diagnosis of carcinoma of the prostate gland. Sapathaty et al. [51] stated that with regard to clinical impact of the radiology imaging, Gallium-68-labeled PSMA PET/CT scan had high diagnostic accuracy for the initial identification of carcinoma of the prostate gland in patients who have clinical or biochemical findings that are suspicious for the diagnosis prostatic cancer as well as it has potential utility as a rule-out test for these patients.

Schiller et al. [52] stated that many patients tend to experience recurrence of carcinoma of the prostate gland pursuant to radical prostatectomy. Schiller et al. [52] visually analysed typical patterns of lymph node (LN) involvement in prostate cancer (PCa) patients who develop biochemical recurrence pursuant to radical prostatectomy and lymphadenectomy by the creation of a colour-coded heat map with the utilization of gallium-68 prostate-specific membrane antigen positron emission tomography (^{68}Ga-PSMA-PET) radiology imaging. Additionally, they did assess which LNs were covered by the Radiation Therapy Oncology Group (RTOG) clinical target volume contouring guidelines. Schiller et al. [52] stated that they had retrospectively screened a total of 1653 ^{68}Ga-PSMA-PET/computed tomography (CT) datasets. Following the meeting of the eligibility criteria, they did include in the study 233 patients who had 799 lymph node (LN) metastases. Schiller et al. [52] created a comprehensive three-dimensional colour-coded lymph node (LN) atlas. They additionally assessed the coverage of lymph node (LN) metastases by RTOG CTV and they performed stratification for risk factors. Schiller et al. [52] summarized the results and the limitations of the study as follows:

- On the whole, mainly high-risk, collective, complete coverage by the standard RTOG CTV had been accomplished in 31.0% of all lymph node (LN) metastases.
- The vast majority lymph nodes (LNs) that were uncovered were found to be situated within the para-aortic, para-rectal, para-vesical, pre-acetabular, pre-sacral, as well as inguinal regions.
- With regard to the examined stratification factors, serum prostate-specific antigen (PSA) levels at the time of the undertaking of PET/CT radiology imaging did have the highest predictive value for extra-pelvic metastatic lymph node (LN) spread.
- Every increase of 1 ng/mL in serum PSA level does raise the risk for the development of metastases outside the CTV by a factor of 1.43.

Schiller et al. [52] made the ensuing summations:

- They had developed the first lymph node (LN) atlas for patients who have recurrent prostate cancer (PC) with the utilization of a heat map technique, so as to illustrate hot spots of lymph node (LN) recurrence.
- The vast majority of detected lymph nodes (LNs) tend not to be covered by standard CTV as recommended by the RTOG.
- Application of the standard RTOG CTV for pelvic irradiation in the salvage setting for high-risk prostate cancer (PCa) patients does seem not to be appropriate.

Conclusions

PET/CT Scan is a very useful imaging modality that detects localized and distant metastases in biochemical recurrence of prostate cancer and this modality of imaging should be used more often from now onwards. CT scan would usually detect nodes/lesions that measure 1 cm or larger but PET/CT scan would detect smaller sized lesions at slightly raised levels of serum PSA. The detection of small localized metastasis at a slightly elevated serum PSA values would make it easier for a second-line treatment of curative intent in the form of salvage lymphadenectomy or salvage radiotherapy targeted at the lesion. Perhaps PET/CT scan should be the first-line imaging modality which should be used in investigating biochemical recurrence and this should be done when the serum PSA is slightly elevated. Further research would be required regarding additional modifications that should be made in the utilization of the various types of PET/CT scan to ascertain if further improvements could be achieved in improving further the detection of smaller prostatic primary tumours as well as metastatic lesions.

Conflict of Interest

None

Acknowledgement

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References

1. Rawla P. (2019) Epidemiology of Prostate Cancer. World J Oncol. 10(2):63-89. doi: 10.14740/wjon1191. Epub 2019 Apr 20. PMID: 31068988.
2. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. (2018) Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 68(6):394-424.
3. Ferlay J E M, Lam F, Colombet M, Mery L, Pineros M, Znaor A, Soerjomataram I. et al. Global cancer observatory: cancer today. Lyon, France: International Agency for Research on Cancer.
4. Panigrahi GK, Praharaj PP, Kittaka H, Mridha AR, Black OM, Singh R, Mercer R, van Bokhoven A, Torkko KC, Agarwal C, Agarwal R, Abd Elmageed ZY, Yadav H, Mishra SK, Deep G. (2019) Exosome proteomic analyses identify inflammatory phenotype and novel biomarkers in African American prostate cancer patients. Cancer Med. 8(3):1110-1123.
5. Ferlay J E M, Lam F, Colombet M, Mery L, Pineros M, Znaor A, Soerjomataram I. et al. Global cancer observatory: cancer tomorrow. Lyon, France: International Agency for Research on Cancer.
6. Chan J M, Gann P H, Giovannucci E L. (2005) Role of diet in prostate cancer development and progression. J Clin Oncol. 23(32):8152-60.
7. Giovannucci E, Rimm EB, Colditz GA, Stampfer MJ, Ascherio A, Chute CG, Willett WC. (1993) A prospective study of dietary fat and risk of prostate cancer. J Natl Cancer Inst. 85(19):1571-9.
8. Kolonel LN, Nomura AM, Cooney RV. Dietary fat and prostate cancer: current status. J Natl Cancer Inst. 1999 Mar 3;91(5):414-28.
9. Platz EA, Leitzmann MF, Michaud DS, Willett WC, Giovannucci E. (2003) Interrelation of energy intake, body size, and physical activity with prostate cancer in a large prospective cohort study. Cancer Res. 63(23):8542-8.
10. Willis MS, Wians FH. (2003) The role of nutrition in preventing prostate cancer: a review of the proposed mechanism of action of various dietary substances. Clin Chim Acta. 330(1-2):57-83.
11. Wikipedia, the free encyclopedia. PET-CT
12. Ulaner GA. (2019) PET/CT for Patients With Breast Cancer: Where Is the Clinical Impact? AJR Am J Roentgenol. 213(2):254-265.
13. Strohl MP, Ha PK, Flavell RR, Yom SS. (2021) PET/CT in Surgical Planning for Head and Neck Cancer. Semin Nucl Med. 51(1):50-58.
14. Calvo FA. (2007) PET-TAC en Oncología: una extraordinaria oportunidad asistencial, docente e investigadora [PET-CT scan in Oncology: an extraordinary health care, teaching and investigator opportunity]. Rev Esp Med Nucl. 26(2):67-8.
15. Fonti R, Conson M, Del Vecchio S. (2019) PET/CT in radiation oncology. Semin Oncol. 46(3):202-209.
16. Krengli M, Milia ME, Turri L, Mones E, Bassi MC, Cannillo B, Deantonio L, Sacchetti G, Brambilla M, Inglese E. (2010) FDG-PET/CT imaging for staging and target volume delineation in conformal radiotherapy of anal carcinoma. Radiat Oncol. 5:10.
17. Goldstein J, Even-Sapir E, Ben-Haim S, Saad A, Spieler B, Davidson T, Berger R, Weiss I, Appel S, Lawrence YR, Symon Z. (2017) Does Choline PET/CT Change the Management of Prostate Cancer Patients With Biochemical Failure? Am J Clin Oncol. 40(3):256-259.
18. Raylman, (1991) Raymond Robert Reduction of positron range effects by the application of a magnetic field: For use with positron emission tomography.
19. Townsend DW. (2008) Combined positron emission tomography-computed tomography: the historical perspective. Semin Ultrasound CT MR. 29(4):232-235.
20. Nutt R. (2002) The History of Positron Emission Tomography. Molecular Imaging & Biology. 4(1): 11-26.
21. Kalender, W.A. (2005) Computed Tomography: Fundamentals, System Technology, Image Quality, Application. Wiley, Erlangen-Nürnberg, 135.
22. Wallitt K L, Khan S R, Dubash S,Tam H H, Khan S, Barwick T D. (2017) Clinical PET Imaging in Prostate Cancer. Radiographics. 37(5): 1512 – 1536.
23. National Comprehensive Cancer Network. Recent updates to NCCN clinical practice guidelines in oncology (NCCN Guidelines®): prostate cancer—version 1.2017. National Comprehensive Cancer Network website.
24. Mottet N, Bellmunt J, Briers E et al. EAU prostate cancer guidelines (2017) European Association of Urology website.
25. Mottet N, Bellmunt J, Bolla M, Briers E, Cumberbatch MG, De Santis M, Fossati N, Gross T, Henry AM, Joniau S, Lam TB, Mason MD, Matveev VB, Moldovan PC, van den Bergh RCN, Van den Broeck T, van der Poel HG, van der Kwast TH, Rouvière O, Schoots IG, Wiegel T, Cornford P. (2017) EAU-ESTRO-SIOG Guidelines on Prostate Cancer. Part 1: Screening, Diagnosis, and Local Treatment with Curative Intent. Eur Urol. 71(4):618-629.
26. Ceci F, Schiavina R, Castellucci P, Brunocilla E, Fuccio C, Colletti PM, Ferretti A, Chondrogiannis S, Rubello D, Romagnoli D, Malizia C, Martorana G, Fanti S. (2013) 11C-choline PET/CT scan in patients with prostate cancer treated with intermittent ADT: a sequential PET/CT study. Clin Nucl Med. 38(7):e279-282.
27. Souvatzouglou M, Eiber M, Takei T, Furst S, Maurer T, Gaertner F, Geinitz H, Drzezgea A, Ziegler S, Nekolla S, Rummeny E J, Schwaiger M, Beer A. (2013) Comparison of intergrated whole-body [(11)C] choline PET/MR with PET/CT in patients with prostate cancer European Journal of nuclear medicine and molecular imaging; 40(10): 1486-1499.
28. Kang P M, Seo W I, Lee S S, Bae S K, Kwak H S, Min K, Kim W, Kang D. (2014) II Incidental abnormal FDG uptake in the prostate on 18-fluoro—2-deoxyglucose positron emission tomography –computed tomography scans. Asian Pacific journal of cancer prevention Asian Pacific Journal of Cancer Prevention: 15(20): 8699-8703 1513-7368.
29. Hodolic M, Maffione A M, Fettich J, Gubina B, Cimitan M, Rubello D. (2013) Metastatic prostate cancer proven by (18) F-FCH PET/CT staging scan in patient with normal PSA but high PSA doubling time. Clinical nuclear medicine; 38(9): 739-740.
30. Vargas H A, Wassberg C, Fox J J, Wibmer A, Goldman D A, Kuk D, Gonen M, Larson S M, Morris M J, Scher H I, Hricak H. (2014) Bone metastasis in castration-resistant prostate cancer: associations between morphologic CT patterns, glycolytic activity, and androgen receptor expression on PET and overall survival. Radiology ; 271(1): 220-229.
31. Buchegger F, Garibotto V, Zilli T, Allainmat L, Jorcano S, Vees H, Rager O, Steiner C, Zaidi H, Seimbille Y, Ratib O, Miralbell

R. (2014) First imaging results of an intra-individual comparison of (11)C-acetate and(18)Ffluorocholine PET/CT in patients with prostate cancer at an early biochemical first or second relapse after prostatectomy or radiotherapy. European journal of nuclear medicine and molecular imaging; 41(1): 68-78.

32. Castelluci P, Ceci F, Graziani T, Schiavina R, Brunoccilla E, Mazzarotto R, Pettinato C, Celli M, Lodi F, Fanti S. (2014) Early biochemical relapse after radical prostatectomy: which prostate cancer patients may benefit from a restaging 11C-choline PET/CT scan before salvage radiation therapy? Journal of nuclear medicine: official publication, Society of Nuclear Medicine ; 55(9): 1424-1429
33. Poulsen M H, Petersen H, Hollund-Carsen P F, Jacobson J S, Gerke O, Karlstoft J, Steffanssen S I, Walter S. (2014) Spine metastases in prostate cancer: comparison of technetium-99m-MDP whole-body bone scintigraphy, [(18)Fcholine positron emission tomography (PET) / computed tomography (CT) and [(18)F-fluoromethylcholine (FCH) positron emission tomography (PET)/ computed tomography (CT) and [(18)F Na F PET/CT BJU International ; 114(6): 818-823.
34. Evangelista L, Cimitan M, Zattoni F, Guttilla A, Zattoni F, Saladini G. (2015) Comparison between conventional imaging (abdominal-pelvic computed tomography and bone scan) and [(18)F]choline positron emission tomography/computed tomography imaging for the initial staging of patients with intermediate- to high-risk prostate cancer: A retrospective analysis. Scandinavian Journal of Urology; 49(5): 345-353.
35. Suardi N, Gandaglia G, Gallina A, Di Trapani E, Scattioni V, Vizziello D, Cucchiara V, Bertini R, Colombo R, Picchio M, Giovacchini G, Montorsi F, Briganti A. (2015) Long-term outcome of salvage lymph node dissection for clinically recurrent prostate cancer: results of a single-institution series with a minimum follow-up of 5 years. European Urology; 67(2): 299-309.
36. Rowe S P, Mana-ay M, Javadi M S, Szabo J Z, Leal J P, Pomper M G, Pienta K J, Ross A E, Gorin M A. (2016) PMSA-Based Detection of Prostate Cancer Bone Lesions With ^{18}F DCFPyL PET/CT: A sensitive Alternative To planar ^{99m} TC MDP Bone Scan, Na^{18}F PET/CT? Clinical Genitourinary Cancer; 14(1): e115-e118.
37. Agarwal K K, Tripathi M, Kumar R, Bal C. (2016) Metastatic super-scan in prostate carcinoma on gallium-68-prostate-specific membrane antigen positron emission tomography/computed tomography scan. Indian J Nucl Med; 31(2): 150-151
38. Su H-Y, Chen M-L, Hsieh P-J, Hsieh T-S, Chao I-M. (2016) Lung Metastasis From Prostate Cancer Revealed by 18F-FDG PET/CT Without Osseous Metastasis On Bone Scan Clinical Nuclear Medicine; 41(5): 392-393.
39. Tong A K T, Zhang Z X, Zaheer S, Yan S X. (2016) Dual-phase (18)F-fluorocholine PET/CT to detect locoregional recurrence of prostate cancer: comparison between each time point of imaging and a summation scan. Clinical imaging; 40(3): 486-489.
40. Apolo A B, Lindenberg L, Shih J H, Mena E, Kim J W, Park J C, Alikhani A, Mckinney Y Y, Weaver J, Turkbey B, Parnes H L, Wood L V, Madan R A, Gulley J L, Dahut W L, Kurdziel K A, Choyke P L. (2016) Prospective Study Evaluating Na18F PET/CT in Predicting Clinical Outcome and Survival in Advanced Prostate Cancer. Journal of nuclear medicine Official publication, Society of Nuclear Medicine ; 57(6): 886-892.
41. Lavalaye J, Kaldeway P, Van Mellick H H E. (2016) Diffuse bone metastases on (68)Ga-PSMA PET/CT in a in a patient with prostate cancer and normal bone scan. Journal of nuclear medicine and molecular imaging; 43(8): 1563-1564.
42. Graziani T, Ceci F, Polverari G, Lima G M, Lodi F, Morganti A G, Ardizzoni A, Schiavina R, Fanti S. (2016) (11)Choline PET/CT for restaging prostate cancer: Ressults from 4,426 scans in a single-centre patient series. European journal of nuclear medicine and molecular imaging; 43(11): 1971-1979.
43. Paone G, Treglia G, Bongiovanni M, Ruberto T, Ceriani L, Giovanolla L. (2013) Incidental detection of Hurtle cell adenoma by 18-choline PET/CT scan in a patient with prostate cancer. Revista espanola de medicina nuclear e imagen molecular; 32(5): 340-341.
44. Oprea-Lager D E, Kramer G, Van De Ven P M, Van Den Eertwegh A J M, Van Moorselaar R J A, Schober P, Hoekstra O S, Lammerstma A A, Boellaard R. (2016) Repeatability of Quantitative 18F-Fluromethylcholine PET/CT Studies in Prostate Cancer Journal of nuclear medicine, Official publication, Society of Nuclear Medicine; 57(5): 721 – 727.
45. Daniela E. (2016) Oprea-Lager, Gem Kramer, Peter M. van de Ven, Alfons J.M. van den Eertwegh, Reindert J.A. van Moorselaar, Patrick Schober, Otto S. Hoekstra, Adriaan A. Lammertsma and Ronald Boellaard Journal of Nuclear Medicine May, 57 (5) 721-727.
46. Morris MJ, Rowe SP, Gorin MA, Saperstein L, Pouliot F, Josephson D, Wong JYC, Pantel AR, Cho SY, Gage KL, Piert M, Iagaru A, Pollard JH, Wong V, Jensen J, Lin T, Stambler N, Carroll PR, Siegel BA; CONDOR Study Group. Diagnostic Performance of ^{18}F-DCFPyL-PET/CT in Men with Biochemically Recurrent Prostate Cancer: Results from the CONDOR Phase III, Multicenter Study. Clin Cancer Res.
47. Roberts, M.J., Morton, A., Donato, P. et al. (2021) ^{68}Ga-PSMA PET/CT tumour intensity pre-operatively predicts adverse pathological outcomes and progression-free survival in localised prostate cancer. Eur J Nucl Med Mol Imaging ; 48, 477-482.
48. Fanti, S., Goffin, K., Hadaschik, B.A. et al. (2021) Consensus statements on PSMA PET/CT response assessment criteria in prostate cancer. Eur J Nucl Med Mol Imaging 48, 469-476.
49. Jansen, B.H.E., Bodar, Y.J.L., Zwezerijnen, G.J.C. et al. (2021) Pelvic lymph-node staging with ^{18}F-DCFPyL PET/CT prior to extended pelvic lymph-node dissection in primary prostate cancer - the SALT trial -. Eur J Nucl Med Mol Imaging 48, 509-520.
50. Afshar-Oromieh, A., da Cunha, M.L., Wagner, J. et al. (2021) Performance of [^{68}Ga]Ga-PSMA-11 PET/CT in patients with recurrent prostate cancer after prostatectomy-a multi-centre evaluation of 2533 patients. Eur J Nucl Med Mol Imaging.
51. Baucknehtt, M., Bertagna, F., Donegani, M.I. et al. (2021) The prognostic power of 18F-FDG PET/CT extends to estimating systemic treatment response duration in metastatic castration-resistant prostate cancer (mCRPC) patients. Prostate Cancer Prostatic Dis.
52. Klingenberg S, Mads R. (2021) Jochumsen, Benedicte P. Ulhøi, Jacob Fredsøe, Karina D. Sørensen, Michael Borre and Kirsten Bouchelouche. Journal of Nuclear Medicine February, 62 (2) 214-220.
53. Satapathy S, Singh H, Kumar R, Mittal BR. (2021) Diagnostic Accuracy of ^{68}Ga-PSMA PET/CT for Initial Detection in Patients with Suspected Prostate Cancer: A Systematic Review and Meta-Analysis. AJR Am J Roentgenol. 216(3):599-607.
54. Schiller K, Stöhrer L, Düsberg M, Borm K, Devecka M, Vogel M M E, Tauber R, Heck M M, Rauscher I, Eiber M, Gschwend J E, Duma M N, Combs S E. (2021) PSMA-PET/CT-based Lymph Node Atlas for Prostate Cancer Patients Recurring After Primary Treatment: Clinical Implications for Salvage Radiation Therapy. Eur Urol Oncol. 4(1):73-83.

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