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PET/CT with ^{18}F-PSMA in Patients with Prostate Cancer, Review of the Initial Experience

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Abstract

METHOD: We carry out an observational study where reviewed the PET/CT studies with PSMA marked with Fluor-18 (^{18}F) carried out from February 2019 to September 2020. We analyzed the average value of hepatic uptake SUV lean average (SUVlave), acquisition time, age, reason from the study, focal, multifocal and diffuse prostate uptake, analysis of the location of metastases, level of prostate specific antigen (PSA), we describe uptakes of non-prostate origin and focal uptakes in ribs without anatomical representation. **RESULTS:** The average hepatic SUVlave was 9.7, the acquisition times were variable (52 - 183 minutes) without alterations in the white-background relationship, the most frequent indication for the study was staging, the uptake in ribs without anatomical representation were considered benign with certain characteristics, PET/CT has the ability to detect neoplastic activity with low PSA levels in lymph nodes < 5 mm and bone metastatic status. **CONCLUSION:** PET/CT with ^{18}F-PSMA has advantages over bone scan and computed tomography of the abdomen and pelvis for the staging of prostate cancer.

Keywords

^{18}F-PSMA, Prostate Cancer, Non-Prostatic Uptakes

1. Introduction

Prostate cancer is a malignant neoplasm that occurs in older men [1]. In Mexico, it ranks second in causes of death from cancer, after lung [2].

Risk factors include age, since most of the prostate cancer diagnosis appears in men over 64 years of age, first-degree family history, black African-American

race, and a high-fat diet [3].

The diagnosis is determined by the prostate specific antigen (PSA), the Gleason score and the extent of the tumor. Various imaging methods are used for initial staging. Magnetic resonance imaging (MRI) shows promising results in locating the tumor and improves the precision of ultrasound-guided biopsy [4], however, despite the fact that European guidelines recommend the use of magnetic resonance imaging in the event that the tumor does not affect other organs, the images suffer from a certain limitation, especially in the central and transition areas [5] [6].

1.1. Prostate Specific Membrane Antigen (PSMA)

Prostate specific membrane antigen (PSMA) is a transmembrane glycoprotein type II, encoded in the follolate hydrosylase 1 gene, also known as the transmembrane glutamate II gene [7]. It is expressed in surface cells of normal prostate tissue and overexpressed in prostate cancer. Its expression increases in high-grade metastatic prostate cancer, in dedifferentiated and resistant to castration [8]. In 2012, Afshar-Oromieh and collaborators at the University Hospital of Heidelberg in Germany, expose for the first time PET/CT images with PSMA, labeled with Galio-68 (^{68}Ga-PSMA) [9].

The physiological biodistribution of ^{68}Ga-PSMA occurs in the lacrimal, salivary glands, small intestine, liver, spleen and in the proximal tubule of the kidney; there is also a significant accumulation of the radiotracer in the ureters and in the bladder due to renal excretion [10] However, among the disadvantages of ^{68}Ga-PSMA is its intense accumulation in the bladder, which can make it difficult to see in the prostate. These results led to the search for other radioisotopes to mark PSMA, finding in ^{18}F-PSMA a lower renal excretion and a longer half-life (^{68}Ga: 68 min vs ^{18}F: 110 min), which allows better availability, and finally, the energy of ^{18}F (0.65 MeV) is lower compared to that of ^{68}Ga (1.90 MeV), which improves spatial resolution [11] (**Figure 1**).

1.2. Initial Staging in High-Risk Patients

Initial staging in high-risk patients due to the fact that in patients with intermediate or high risk prostate cancer, the metastatic nodes may be smaller than 8 mm, the imaging methods (MRI and CT) continue to be of low sensitivity, since they only evaluate size [12]. Primary staging with PET/CT with PSMA has shown greater sensitivity and specificity for extension to metastatic nodes [13] [14], improving the detection of metastatic disease with low levels of PSA (<0.2 ng/mg) and can detect nodes between 3 at 10 mm, these would go unnoticed by CT [12].

TNM Classification [15]

Primary tumor:

- Tx: The presence of the primary tumor cannot be assessed.
- T0: There is no evidence of a primary tumor.

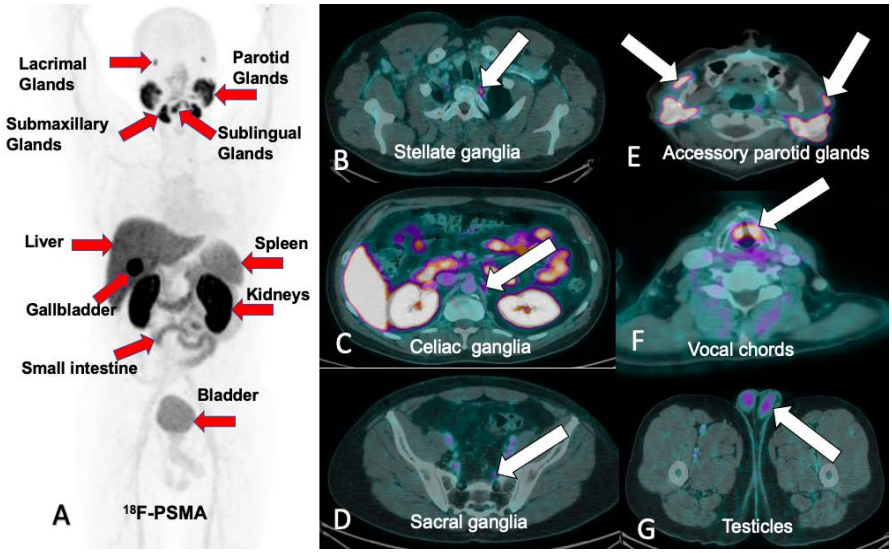

Figure 1. General description of the physiological uptakes with ^{18}F-PSMA. (A) MIP in anterior showing physiological uptake in the lacrimal, parotid, submaxillary and sublingual glands, liver, gallbladder, spleen, small intestine and bladder (red arrows). PET/CT fusion in axial section with physiological uptakes in (B) stellate ganglia (C) celiac ganglia (D) presacral ganglia (E) bilateral accessory parotid glands (F) vocal cords and (G) testes.

- T1: Clinically inapparent tumor (not palpable or visible by imaging techniques).
- T2: Tumor confined to the prostate.
- T3: Tumor that extends beyond the prostatic capsule.
- T4: The tumor invades adjacent organs other than the seminal vesicles.

Lymph node Involvement:

- Nx: Lymph node involvement cannot be assessed.
- N0: Absence of lymph node involvement
- N1: Regional node metastases.

Distant metastasis:

- Mx: The existence of distant metastases cannot be assessed.
- M0: Absence of distant metastasis.
- M1: Distant metastasis (**Figure 2**).

Bone metastases are among the main causes of pain and death in patients with prostate cancer, the degree of bone involvement is essential to define the best treatment strategy [16]. Prostate adenocarcinoma most commonly spreads to well-vascularized bone structures, such as the spine, ribs, skull, and proximal ends of long bones [17].

PET/CT with PSMA shows potential for the detection of bone metastases in patients with prostate cancer, positron emission tomography has shown superiority over bone scintigraphy to determine a generalized condition [18] (**Figure 3**).

1.3. Non-Prostatic Pathologies with PSMA Uptake

The expression of PSMA is found in both malignant and benign non-prostatic

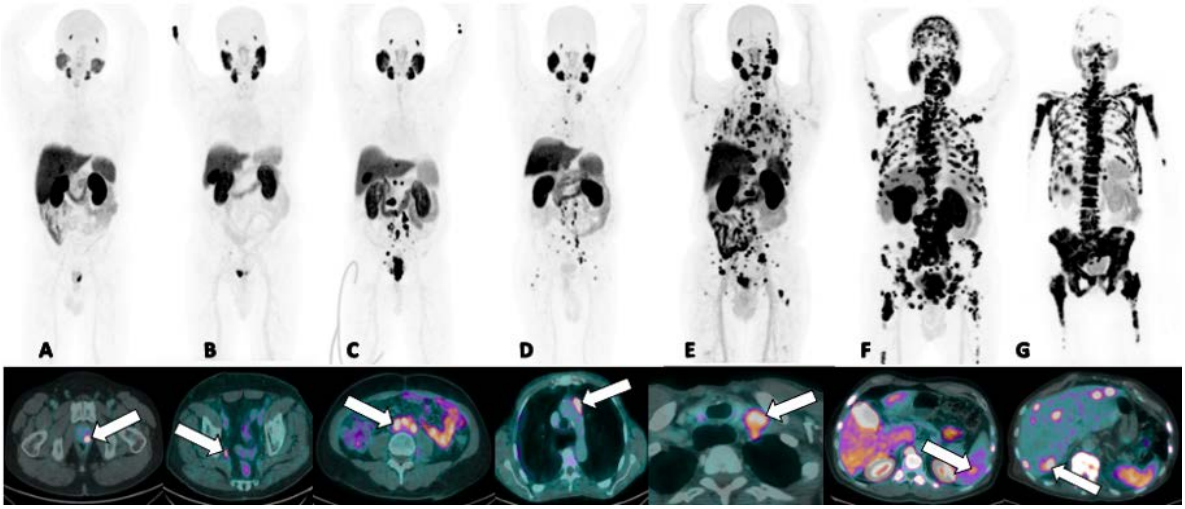

Figure 2. PET images with ^{18}F-PSMA in anterior MIP and fusion in axial section with uptake in (A) focal in prostate (B) prostate with right iliac ganglion (C) prostate with pelvic and retroperitoneal lymphadenopathy (D) multiple bilateral inguinal, pelvic, retroperitoneal, mediastinal and cervical lymphadenopathy (E) prostate, pelvic, retroperitoneal, mediastinal, cervical, axillary lymph nodes, pulmonary nodules, and multiple bone metastases in the axial and appendicular skeleton (F) prostate, pelvic, retroperitoneal, cervical, axillary, pulmonary nodules, multiple bone metastases in axial and appendicular skeleton in the spleen. Is to notice the absence in the uptake of the right submaxillary glandular. (G) prostate, pelvic and retroperitoneal lymphadenopathy, extensive bone metastases in the axial and appendicular skeleton (super scan) and liver metastasis.

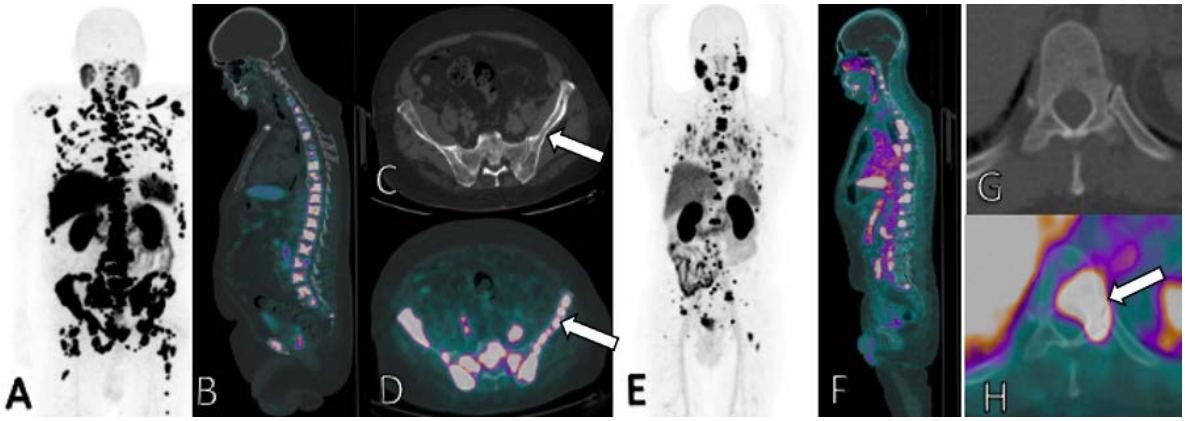

Figure 3. male patient with a 2-month history of lumbar pain and PSA of 233 ng/dl (A) MIP in anterior projection with uptake in the prostate and extensive lymph node and bone tumor burden. (B) PET/CT fusion in a sagittal section where we observe the spine with multiple lesions with intense radiopharmaceutical uptake. (C) and (D) CT and fusion in an axial section at the pelvis level with lytic lesions in both iliac and sacral intense uptake bones (white arrows). A 70-year-old male patient who attended staging for prostate cancer, at the time of the study had PSA of 110 ng/mg; (E) MIP in anterior projection with multiple lesions with intense uptake of diffuse distribution in the axial and appendicular skeleton. (F) PET/CT fusion with bone window in sagittal section; the spine is seen with multiple focal ^{18}F-PSMA uptakes. (G) CT and (H) fusion with PET shows intense radiopharmaceutical uptake involving body, peduncle, and left facet without anatomical representation (white arrow).

pathologies, this situation determines difficulties in interpretation [19] to differentiate prostate cancer metastases from other primary malignant neoplasms [20]. This is because PSMA is expressed in the endothelial cells of the neovasculatures of solid tumors, but not in the endothelial cells of normal vessels [21].

2. Objective General

- Review of the initial experience in the use of PET/CT with ^{18}F-PSMA.
- Average value of hepatic uptake SUV Lean average (SUVlave).
- Age.
- Analysis of the location of metastases.
- Describe and divide the uptakes of non-prostatic tumors and the focal uptakes in the rib without anatomical representation with ^{18}F-PSMA.
- Determine the relationship between the level of prostate specific antigen (PSA) and positive uptakes for prostate cancer, by PET/CT with ^{18}F-PSMA.
- Reason for the study.
- Focal, multifocal or diffuse prostate.
- APE level.

2.1. Justification

In February 2019, we started the use of PET/CT with ^{18}F-PSMA, this work will allow us to show our initial experience with this radiopharmaceutical, observe the spread of prostate cancer, and document uptakes of non-prostatic origin.

2.2. Methodology

A retrospective analysis was performed, in which patients undergoing PET/CT with ^{18}F-PSMA from February 2019 to September 2020 were studied at the CT Scanner San Ángel, Mexico City.

Inclusion criteria: patients with PET/CT study with ^{18}F-PSMA and complete file.

Exclusion criteria: patients with an incomplete file.

A total of 393 studies were conducted, 21 patients were excluded due to incomplete records. In total, 372 studies in 252 patients were analyzed.

The patients signed informed consent to carry out the study.

Definition of variables and measurement scales (Table 1).

3. Results

In the age analysis, we observed that the average was 70.2 years, median 70 and a mode of 73 years. The youngest patient was 42 years old and the oldest patient was 93 (Table 2).

Table 1. Definition of variables and measurement scales.

VARIABLE	CONCEPTUAL DEFINITION	OPERATIONAL DEFINITION	TYPE OF VARIABLE
Average liver uptake value (SUV Lean average).	Used to compare the standardized value of uptake with lesions.	It is obtained by placing an VOI in the right lobe of the liver, this used as a reference value.	Quantitative
Age Independent of the presentation of prostate cancer.	Age Years completed at the time of diagnosis.	It is obtained by ordering the patients by age group.	Quantitative
Reason for the indication of the study.	Valid Reason for Using the ^{18}F-PSMA Diagnostic Test	It is obtained from patient records.	Quantitative

Continued

Focal, multifocal, or diffuse prostatic uptake.	Location of the primary tumor (right or left lobe or both)	Based on the record obtained from the nuclear medicine report.	Quantitative
PET/CT studies, positive, negative.	Case numbers.	Based on the records obtained in the database.	Quantitative
APE level.	A protein produced by the cells of the prostate glands, its concentration in the blood is measured.	The results were obtained from the files.	Quantitative
Analysis based on the location of metastases.	Spread of prostate cancer to lymph nodes and organs.	Based on the PET/CT results, the anatomical location of the metastases was determined.	Quantitative
Non-prostatic tumor uptakes.	Standardized value of uptake in lesions of non-prostate origin with 18F-PSMA	Based on the record obtained from the nuclear medicine report	Qualitative
Focal uptakes in rib.	Standardized uptake value in ribs without anatomical representation.	Based on uptake rib focal only and determined predicter factors.	Qualitative

Table 2. Demographic data of the patients studied with ^{18}F-PSMA.

Ages grouped by ranges	Number of studies
42 to 51	12
52 to 61	71
62 to 73	134
74 to 82	117
83 to 93	38
Total	372

Mean age = 70 age. Standard deviation = 57.47.

3.1. Average Liver Uptake Value (SUV Lean Average)

In all the studies, we measured the SUVlave at the level of the right liver lobe, finding that the highest value was 21.0, the lowest was 1.1, the average was 9.7, the mode was 10.5 and the median was 9.7.

We also analyzed the post-injection acquisition time of each of the studies performed, the maximum time was 183 minutes, the minimum time was 54 minutes, an average of 86.5 minutes, a median of 83 and a mode of 63 minutes.

3.1.1. Analysis Based on the Primary Uptake of the Prostate and Location of Metastases

The results of the PET/CT with ^{18}F-PSMA were the following: 281 were positive, 87 negative and 4 doubtful.

The prostate uptakes and the distribution of metastases were analyzed, the results were as follows.

Lesion exclusively in the prostate and surgical bed: 81 studies (28.8%) divided into unifocal (30), multifocal (31) and diffuse (20) lesions. Surgical bed with 18 (6.4%).

The highest SUVlmax was 41.1 and the lowest SUVlmax was 2.7 in injuries exclusively to the prostate.

In the surgical bed, the highest SUVlmax was 40.1 and the lowest was 2.7.

Exclusively lymph nodes: 13 (4.6%) studies, in which we found the following:

- 9 Studies with local nodes.
- 1 Study with local + retroperitoneal ganglia.
- 1 Study with local + retroperitoneal + mediastinal nodes.
- 1 Study with local + retroperitoneal + mediastinal + left cervical lymph nodes.
- 1 Study with retroperitoneal + mediastinal lymph nodes.

Exclusively bone metastases: 9 studies (3.2%):

- 1 Study with a single osteoblastic lesion.
- 5 Studies with multiple osteoblastic lesions.
- Studies with multiple lesions without anatomical representation.

Prostate + lymph nodes: 54 (19.2%) studies:

Unifocal: 21 studies:

- 14 Local node studies.
- 5 Local node studies + retroperitoneal.
- 1 Study with retroperitoneal ganglia.
- 1 Study with mediastinal lymph nodes.

Multifocal: 15 studies:

- 7 Local node studies.
- 5 Studies with local + retroperitoneal nodes.
- 2 Studies with local + mediastinal nodes.
- 1 Study with mediastinal lymph nodes.

Diffuse: 18 Studies:

- 10 Local node studies.
- 3 Studies with local + retroperitoneal lymph nodes.
- 1 Study with bilateral retroperitoneal + mediastinal + axillary nodes.
- 2 Studies with retroperitoneal nodes.
- 1 Study with local + retroperitoneal + bilateral cervical nodes.
- 1 Study with local + retroperitoneal + mediastinal + left cervical nodes.

Prostate + bone metastasis: 10 studies (3.55%).

Unifocal: 5 studies:

- 3 Studies with multiple osteoblastic lesions.
- 1 Study with a single metastatic lesion without anatomical representation.
- 1 Study with single osteoblastic lesion.

Multifocal: 4 studies:

- 2 Studies with multiple osteoblastic lesions.
- 1 Study with a single lesion without anatomical representation.
- 1 Study with a single osteolytic lesion.

Diffuse: 1 Study with multiple bone lesion without anatomical representation.

Prostate + lymph nodes + bone metastases: 53 (18.86%) studies.

Unifocal: 17 studies:

- 4 Studies with local lymph nodes + single osteoblastic lesion.

- 3 Studies with local ganglia + multiple osteoblastic lesions.
- 6 Studies with local + retroperitoneal ganglia + multiple osteoblastic lesions.
- 1 Study with local + retroperitoneal ganglia + multiple osteoblastic lesions.
- 1 Study with local lymph nodes + single bone lesion without anatomical representation.
- 1 Study with local + retroperitoneal + mediastinal nodes + single osteoblastic lesion.
- 1 Study with local lymph nodes + left cervical + multiple osteoblastic lesions.

Multifocal: 17 studies:

- 6 With local ganglia + multiple osteoblastic lesions.
- 2 With local lymph nodes + single blastic lesion.
- 1 With local lymph + retroperitoneal + left cervical ganglia + multiple osteoblastic lesions.
- 1 With local lymph + retroperitoneal ganglia + multiple lytic bone lesions.
- 1 With local ganglia + multiple bone lesions without anatomical representation.
- 1 With local nodes + single lytic bone lesion.
- 1 With local retroperitoneal ganglia + single osteoblastic lesion.
- 2 With local nodes + retroperitoneal ganglia + single osteoblastic lesion.
- 1 With local + retroperitoneal ganglia + multiple osteoblastic lesions.
- 1 With local retroperitoneal ganglia + mediastinal + left cervical ganglia and multiple osteoblastic lesions.

Diffuse: 18 studies:

- 2 Studies with local retroperitoneal lymph nodes + single osteoblastic lesion.
- 2 Studies with local ganglia + single lesion without anatomic representation.
- 4 Studies with local lymph node studies + multiple osteoblastic lesions.
- 1 Study with local + retroperitoneal ganglia + single osteoblastic lesion.
- 1 Study with local ganglia + retroperitoneal + mediastinal + multiple osteoblastic nodes.
- 1 Study with local ganglia + retroperitoneal + mediastinal ganglia + multiple osteoblastic and lithic lesions.
- 1 Study with local ganglia + retroperitoneal + multiple bone lesions without anatomical representation.
- 2 Studies with local retroperitoneal nodes + multiple osteoblastic lesions.
- 1 Study with mediastinal lymph nodes + multiple osteoblastic lesions.
- 2 Studies with local lymph nodes + multiple bone lesions without anatomical representation.
- 1 Study with local ganglia + multiple osteolytic lesions.
- 1 Study with local retroperitoneal ganglia + left cervical + multiple bone lesions without anatomical representation.

Ganglion + bone metastasis: 19 studies:

- 1 Study with local lymph nodes + pulmonary hilum + multiple osteolytic lesions.

- 2 Studies with mediastinal lymph nodes + multiple osteoblastic lesions.
- 1 Study with local lymph nodes + multiple osteoblastic lesions.
- 1 Study with local + retroperitoneal + left cervical ganglia + multiple osteolytic lesions without anatomical representation.
- 1 Study with local + retroperitoneal + mediastinal nodes + left pulmonary hilum, left cervical + multiple osteoblastic lesions.
- 2 Studies with local lymph nodes + single osteolytic lesion.
- 1 Study with local + retroperitoneal ganglia + multiple osteoblastic lesions.
- 1 Study with retroperitoneal + mediastinal lymph nodes + multiple osteoblastic and lytic lesions.
- 1 Study with retroperitoneal + mediastinal ganglia + multiple osteoblastic lesions.
- 2 Studies with retroperitoneal lymph nodes + multiple osteoblastic lesions.
- 1 Study with local + retroperitoneal + mediastinal ganglia + multiple osteoblastic and lytic lesions.
- 1 Study with local ganglia + multiple osteoblastic lesions.
- 1 Study with local lymph nodes + retroperitoneal + mediastinal + bilateral cervical nodes + multiple osteoblastic lesions.
- 1 Study with retroperitoneal ganglia + left cervical + multiple osteolytic lesions.
- 1 Study with retroperitoneal ganglia + mediastinal + multiple osteoblastic lesions.
- 1 Study of mediastinal lymph nodes + multiple osteoblastic lesions.

Surgical bed + lymph node: 10 studies (3.55%):

- 8 Local node studies.
- 1 Studies with local + retroperitoneal lymph nodes.
- 1 Study with local + retroperitoneal + left cervical lymph nodes.

Surgical bed + Bone metastases: 5 (1.77%): With multiple osteoblastic lesions.

Surgical bed + lymph nodes + bone metastases: 9 studies (3.2%):

- 1 Study with local + retroperitoneal lymph nodes + single lesion without anatomical representation.
- 1 Study with local + retroperitoneal ganglia and multiple bone lesions without anatomical representation.
- 1 Study with left retroperitoneal + mediastinal + cervical ganglia and single osteoblastic lesions.
- 1 Study with local ganglia + multiple osteoblastic lesions.
- 2 Studies with local + retroperitoneal ganglia + multiple osteoblastic lesions.
- 1 Study with local lymph nodes + single osteoblastic lesion.
- 1 Study with local ganglia + cervical + multiple bone lesions without anatomical representation.
- 1 Study with local retroperitoneal ganglia + multiple osteoblastic and lytic bone lesions (Figure 2).

3.1.2. Particular Discoveries

37 (13.16%) had positive nodes smaller than 5 mm.

27 (9.60%) studies with lymphadenopathy in 38 supradiaphragmatic regions: 12 left cervical nodes, 1 bilateral cervical, 21 mediastinal lymph nodes, 3 in pulmonary hilum and 1 bilateral axillary.

We detected 16 (5.69%) studies with unusual metastases: 7 pulmonary, 3 hepatics, 3 in the penis, 1 splenic, 1 muscular and 1 in the mesorectum (**Figure 4**).

3.1.3. ^{18}F-PSMA PET/CT Results Based on PSA Numbers

Of the 393 studies carried out, we have PSA levels in 181 (45.93%). The minimum PSA value was 0.001 and the highest value was 1789 ng/ml (**Table 3**).

3.1.4. Distribution for Reasons of Request

The reasons for the studies were varied, with staging (144), re-staging (104), assessment of response to treatment (53), surveillance (53) and recurrence (18).

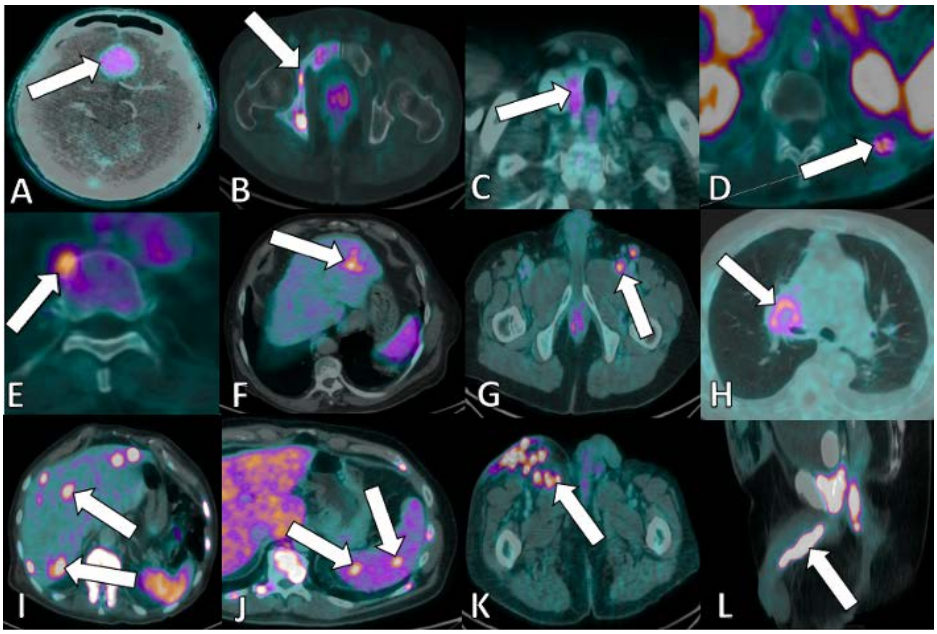

Figure 4. Fusion of PET/CT with ^{18}F-PSMA axial section with examples of uptake of non-prostatic origin and non-usual metastases (A) Skull with extra-axial lesion dependent on the cerebral falx with ^{18}F-PSMA uptake, compatible with meningioma (white arrow). (B) increased density in bone structures of the right hemipelvis associated with heterogeneous uptake (white arrow) in a patient with Paget's disease. (C) Right thyroid lobe with solid nodules with uptake (we have a histological report showing hyperplastic nodules). (D) posterior costal arch fracture with focal radiopharmaceutical uptake. (E) lumbar vertebral body with anterior marginal osteophyte with radiopharmaceutical uptake. (F) lesion in the left liver lobe with uptake of the radiopharmaceutical that suggests malignant etiology (hepatocarcinoma) as the first possibility. (G) known patient with Hodgkin lymphoma shows left inguinal lymphadenopathy with ^{18}F-PSMA uptake. (H) lesion in the right pulmonary hilum with heterogeneous uptake compatible with a second primary neoplasm. Uncommon metastases, (I) hypodense liver lesions with intense uptake (J) spleen with focal uptakes (K) right pelvic limb with implants intense uptake located in the anterior compartment (L) sagittal section with intense linear uptake in the cavernous bodies of the penis.

3.1.5. Non-Prostatic ^{18}F-PSMA Uptake

95 studies (25.5%) with uptake of non-prostatic origin with ^{18}F-PSMA, which we divided into three groups, benign 59 (63%), malignant 9 (9%) and nonspecific 27 (28%) (Table 4, Figure 4).

3.1.6. Focal Uptakes in Ribs without Anatomical Representation

9.6% of the studies (36) presented focal uptakes of the radiopharmaceutical in ribs but without anatomical representation, we have classified them as nonspecific. In the SUVlmax analysis, the highest was 8.2 and the lowest was 1.8 (average of 4.0 and mode of 2.6) (Figure 5).

Table 3. PET/CT results based on PSA level.

PSA ng/ml	PET+	PET−	PET UNCERTAIN
0.001 to 0.01		6	
>0.01 to ≤0.07	2	11	1
≥0.1 to ≤0.5	10	11	
>0.5 to ≤1	6	1	
>1 to ≤5	32	1	1
>5 to ≤10	37	1	2
>10 to ≤15	17	1	
>15 to ≤20	7		
>20	34		
Total	145	32	4

Table 4. In the following table we divide the pathologies of non-prostatic origin with uptake.

Benign	Number of studies	Malignant	Number of studies	Unspecific	Number of studies
Osteodegenerative	19	Urothelial origin	3	Diffuse thyroid uptake	11
Pulmonary nodules	3	Hepatocarcinoma	1	Linear in lung	1
Pulmonary infiltrates	4	Lymphoma	1	Thickening of the rectum	1
Lung consolidation	1	Pancreatic neoplasia	2	Bladder wall	1
Hemangiomas	4	Lung primary	1	Nonspecific osseous	6
Inflammatory esophagus	5	Liposarcoma in pancreas	1	Rib with lytic area	1
Enchondroma	1			Iliac nodes	1
Epididymis	1			Penis	2
Fractures	3			Inguinal ring	1
Atrial lipoma	1			Intestinal polyp	1

Continued

Meningioma	1	Inguinal canal cyst	1
Paget's disease	2		
Fibrocicatricial changes in the lung	2		
Thymoma	1		
Muscular	1		
Adrenal adenoma	1		
Thyroid nodule	1		
Bladder wall	1		
Pleura	1		
Bladder wall	1		
Lymph nodes (axillary, mediastinal and cervical)	5		

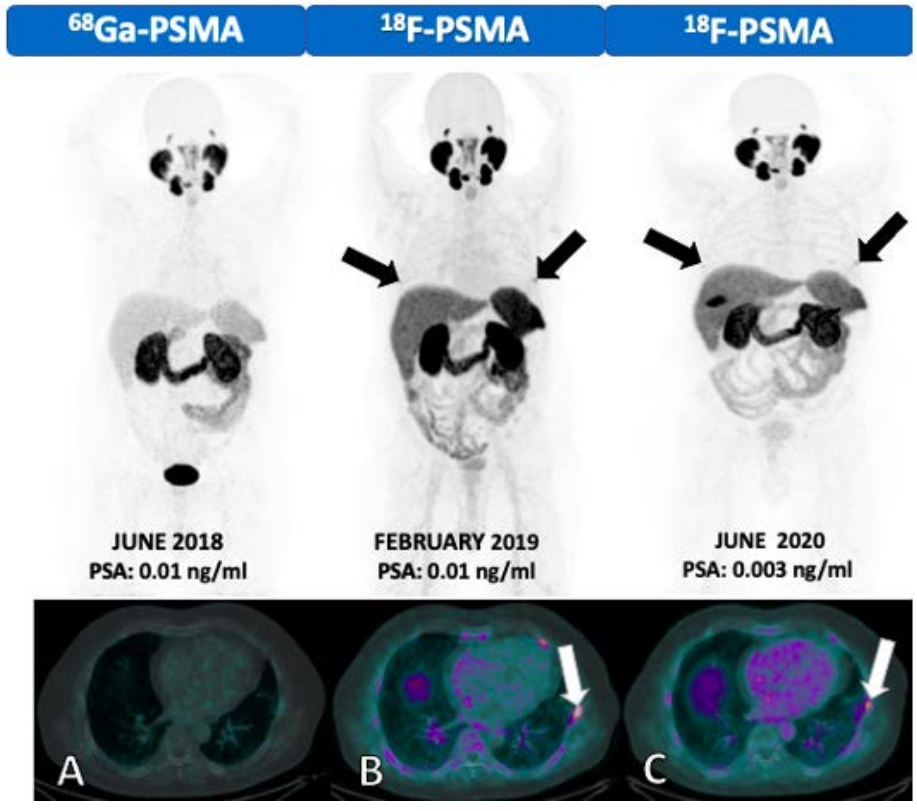

Figure 5. Follow-up of a patient with a history of prostate cancer (A) MIP in anterior and PET/CT in axial fusion with ^{68}Ga-PSMA performed in June 2018 without evidence of abnormal uptakes (B) Follow-up carried out in February 2019 with ^{18}F-PSMA where minimal focal uptake is observed in the sixth bilateral costal arch with SUVlmax of 3.5, the PSA at the time of the study was 0.01 ng/ml. (C) PET/CT with ^{18}F-PSMA performed in June 2020, the focal uptakes in the costal arches continue with minimal uptake and without significant changes in size, the PSA at the moment of the study was 0.003 ng/ml.

4. Discussion

Prostate cancer is the second malignant tumor and the second most frequent cause of death in men, PET/CT with ^{18}F-PSMA has proven to be a fundamental non-invasive technique in the initial staging in high-risk patients, important in the planning of the surgical approach, functional in the planning of radiotherapy, location of the tumor in biochemical recurrence, useful as a guide for biopsy in patients with high suspicion of cancer with negative previous biopsy results, and to assess the response to treatment.

The objective of this study is to evaluate the results obtained in the scans carried out with PET/CT with ^{18}F-PSMA during the period: February 2019 to September 2020.

We measured the SUVlave (SUVLean average) in the liver of each one, the highest value found was 21 and the lowest was 1.1, this last value corresponds to a patient with extensive tumor burden (superscan), we found a mode of 10.5 and an average of 9.7. The liver belongs to the physiological uptake of ^{18}F-PSMA, when placing this reference ROI in the liver, verify that the gallbladder is not included.

The acquisition time of most studies (mode) was 63 minutes. 183 minutes the longest and the shortest at 54 minutes. Although the acquisition times were variable, the analyzes have an appropriate quality, with no alterations in the white background relationship.

The average age was 70.2 years, with a mode of 73 years, 124 patients are in the range of 62 to 73 years, our youngest patient with 42 years and our oldest patient 93 years. Our result agrees with the referenced literature, where age is recognized as a risk factor, since most of the prostate cancer diagnosis appears in men older than 64 years.

In the positive PET/CT, the most frequent involvement was observed in lesion exclusively in the prostate with 29.7% (82) with a predominance of multifocal lesions; second, involvement of the prostate + lymph nodes + bone lesions with 21.2% (58) studies.

Surgical bed + bone metastases and surgical bed + lymph nodes were the least frequent with 8 and 10 studies respectively.

37 studies (13.4%) presented nodes smaller than 5 mm with radiopharmaceutical uptake.

As unusual findings, we found 7 pulmonary metastases, 3 liver, 3 in the penis, 1 splenic, 1 of axillary lymphadenopathy, 8 cervical on the left side and 1 bilateral, 1 nodular lesion in the mesorectum and 1 study in a muscle implant.

Despite the high incidence of prostate cancer, there are few reports of metastatic involvement of the cervical nodes, the predilection for the left side is due to the fact that tumor cells can lodge in the nodes by retrograde spread, due to the proximity of the duct thoracic with left subclavian vein [22].

Hepatic metastases are considered the third site of extra nodal metastases in prostate cancer, after bone and lung; occur in disease refractory to hormonal treatment and in late stages, PSMA uptake in liver metastases may be due to the

diversity of prostate cancer phenotypes, predominantly neuroendocrine transdifferentiation [23]. The spleen and muscle are the least common extra nodal metastasis sites [24].

Most of the reasons for the request were staging with 144 studies.

Of the PET/CT performed we have the PSA value in 179. 18 positive studies with PSA < 1.0, of which the minimum value with positive PET/CT was 0.01 ng/ml.

We documented 89 studies with ^{18}F-PSMA uptake of non-prostatic origin with a predominance in lesions of benign etiology, being the osteodegenerative changes the ones that occurred more frequently, the highest SUVlmax value was 8.5 and the lowest 2.6. Regarding uptakes of non-prostate malignant origin, we present 9 documented studies that present a second primary tumor. In the literature, the association of these uptakes with endothelial neovasculature is well known, showing that PSMA is not exclusive to prostate tissue, this must be taken with relevance, since they can simulate prostate cancer metastasis.

36 studies presented focal uptakes in rib(s) without anatomical representation. In our initial experience, we considered these uptakes as nonspecific, however there was no significant change in size and SUVlmax at follow-up. There is little literature that mentions the nature of these solitary uptake in ribs, however we identified that most of them are of benign origin; taking into account the low uptake of the radiopharmaceutical, the correlation with any signs of trauma and PSA levels [25].

5. Conclusions

- The acquisition times were varied, from 54 to 183 minutes, all studies have adequate quality for interpretation without alterations in the white-background relationship.
- The average hepatic SUVlave is 9.7.
- Staging occupied the highest percentage of PET/CT indication.
- We detected both unifocal and multifocal uptakes in the prostate with PET/CT with ^{18}F-PSMA.
- There are uptakes in both benign and malignant lesions due to its expression in the endothelial cells of the neovasculature, that can cause false positives, it is advisable for the doctor who examines the study to have this knowledge in order to obtain an accurate interpretation. There is little literature on solitary uptakes in ribs without anatomical representation with ^{68}Ga-PSMA. To our best knowledge, this is the first study with ^{18}F-PSMA to evaluate and describe uptakes at the rib level. Our results indicate that these findings are considered benign, when PSA levels and the rest of the study are negative.
- Although there is literature that mentions that liver metastases are not so uncommon (25%, 8%) [24] [26], in the 281 positive studies, 2 patients (3 studies) had hyper-uptake liver metastases (0.71%). Among the findings of one of these two patients, we found PSA of 169 ng/mg, histological report of invasive prostatic adenocarcinoma and extensive tumor burden (superscan),

the patient died 7 months after the first PET/CT, for which reason we agree with the literature that mentions a mortality of 6 to 14 months with this type of lesion [26]. Liver metastases are frequently associated with neuroendocrine transdifferentiation, which is why PET/CT with ^{18}F-FDG is useful in metastatic disease with mutation.

- PET/CT with PSMA has the ability to determine bone metastatic status, there are even hyper-uptake bone metastases that we can detect without anatomical representation. We found 11 studies (3.91%) with hyper-uptake lytic lesions, as well as 12 (4.27%) studies with hyper-uptake bone metastases without anatomical representation. In interesting cases, we have the follow-up of patients in evaluation of response to treatment who show partial response to ^{18}F-PSMA uptake, but with a considerable increase in the number of osteoblastic lesions. This analysis reveals that there may be a disagreement between the functional (PERSIST) and the anatomical (RESIST) assessment; considering that the molecular precedes the morphological (**Figure 6**).
- We have 179 studies correlated with PSA. 10.05% (18 studies) were positive with PSA < 1.0, this demonstrates the ability of ^{18}F-PSMA to detect neoplastic activity with low PSA levels.
- We detected 20 studies (7.2%) with supradiaphragmatic lymphadenopathy, which are not so frequent, however, it should be taken into consideration that they may be present in advanced cases of the disease. Supradiaphragmatic extension occurs by hematogenous spread through the vertebral venous system or Batson's plexus.
- Conventional studies (MRI, ultrasound and CT) have limitations to detect metastatic nodes smaller than 10 mm in the initial staging of patients with high-risk prostate cancer. ^{18}F-PSMA PET/CT has the potential to detect ma-

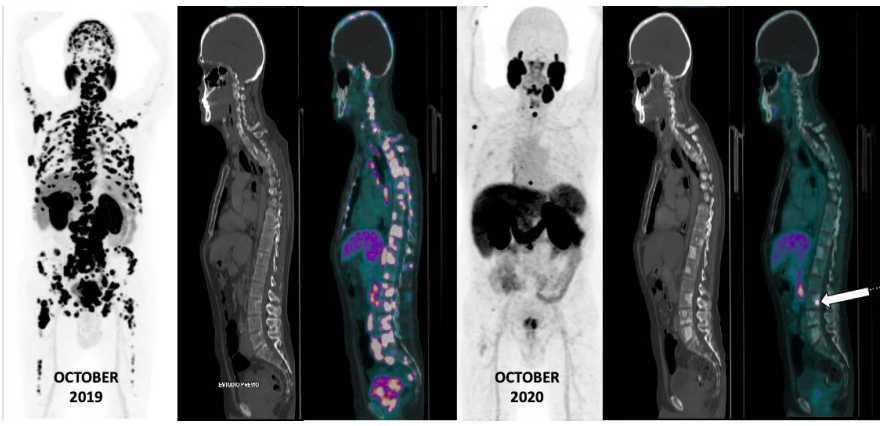

Figure 6. 67-year-old male patient with prostate cancer. MIP in the anterior projection of PET/CT with ^{18}F-PSMA performed in October 2019 (PSA 1789 ng/mg) manifest extensive lymph node tumor burden and predominance in bone; window CT for bone and fusion in the sagittal section with multiple uptakes with poor anatomical representation in the spine. In the PET/CT to assess response to treatment one year later, there is a significant decrease in hyper-uptake bone metastases, however the number of osteoblastic lesions (inactive metastases) increased.

lignant infiltration in nodes smaller than 5 mm, which can be considered normal on anatomical studies

- Considering the previous points, PET/CT with ^{18}F-PSMA has advantages over bone scintigraphy and computed tomography of the abdomen and pelvis for the staging of prostate cancer.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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