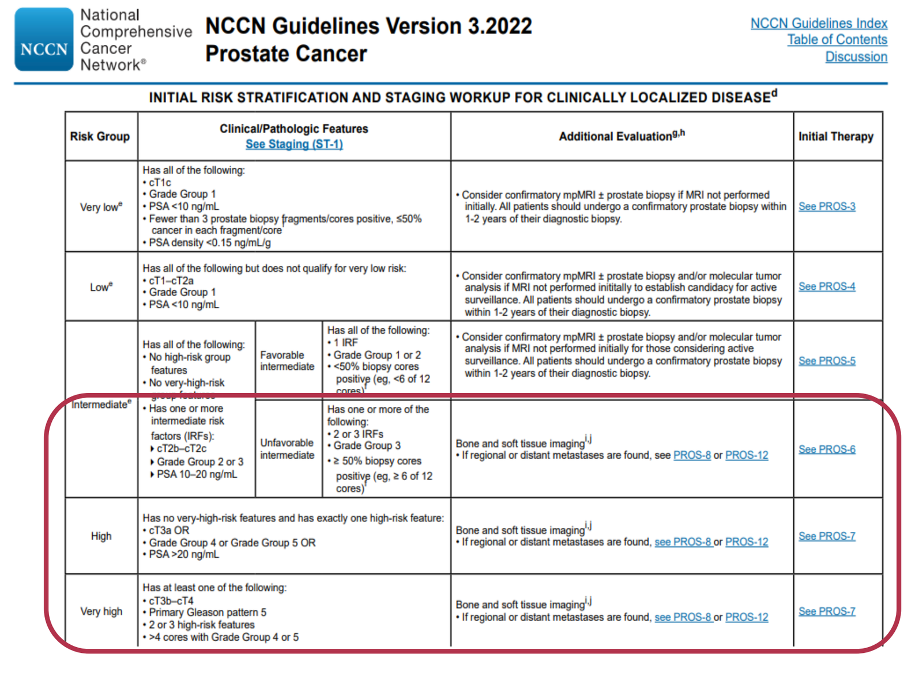
PSMA PET Revolutionizing Prostate Cancer Management

Chiarra M.Thompson MD, Lauren Barnett, Jin Qi MD, Sacha Baldeosingh MD, Sussie DeMello CNMT, Bernard Kamara CNMT, and Irfan Farukhi MD

VA
U.S. Department of Veterans Affairs
Veterans Health Administration
VA North Texas Health Care System

- **Introduction:** Prostate cancer is the most common cancer among men (after skin cancer), but it can often be treated successfully with proper staging and restaging of the disease. Studies have shown that Prostate-specific membrane antigen PSMA PET Imaging can significantly improve how prostate cancer is detected and treated. Recent FDA approval of this imaging agent will prove to be vital in the future management of prostate cancer patients.
- **Purpose:** This educational exhibit will describe the clinical applications, protocol, and interpretation techniques used at our institution and working towards standardization nationwide for PSMA PET Imaging. We will also provide examples of potential pitfalls encountered during image interpretation.
- **Discussion:** PSMA PET Imaging has been shown to be superior to conventional imaging for the staging and restaging of prostate cancer due to improved detection of pelvic lymph nodes and distant metastases. This ultimately results in subsequent adjustments in clinical management.
- **Conclusion:** The staging and particularly the restaging of advanced prostate cancer has traditionally been a challenge for physicians. Recent increased utilization of PSMA PET Imaging has proved to be a promising viable solution to the challenges of this disease.



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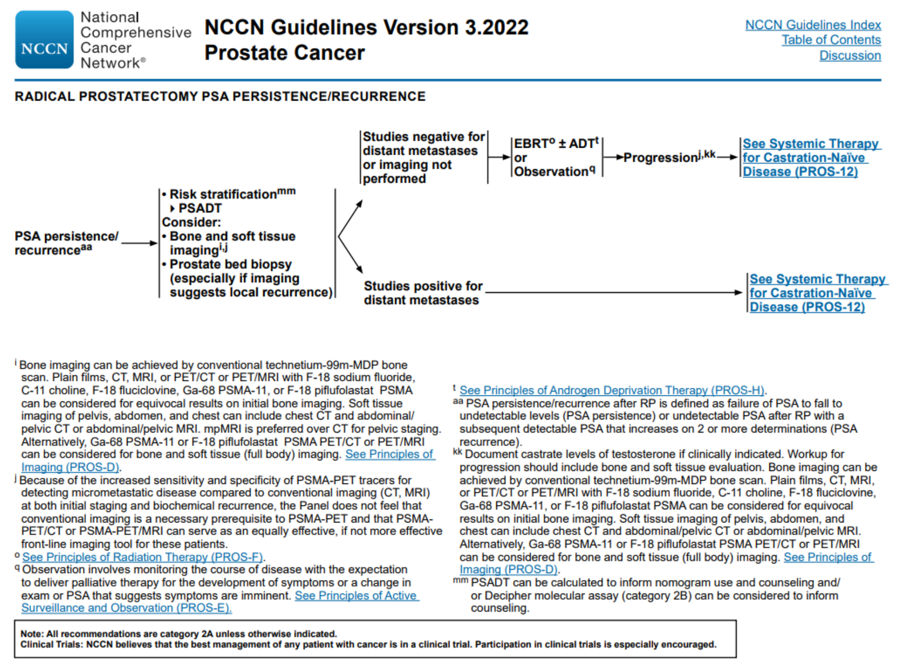
Prostate Cancer
INITIAL RISK STRATIFICATION AND STAGING WORKUP FOR CLINICALLY LOCALIZED DISEASE



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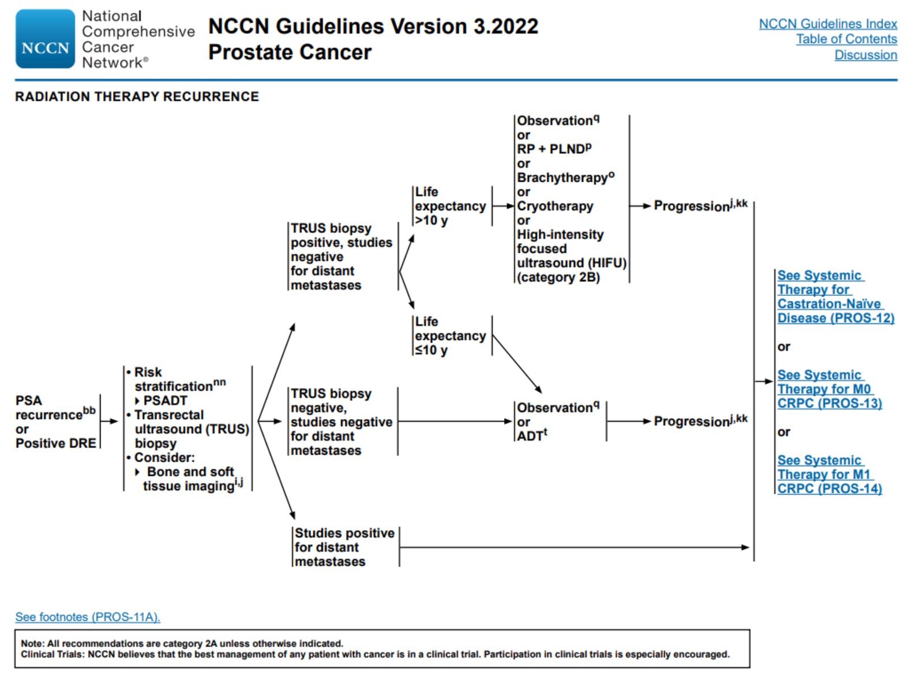
RADICAL PROSTATECTOMY PSA PERSISTENCE/RECURRENCE



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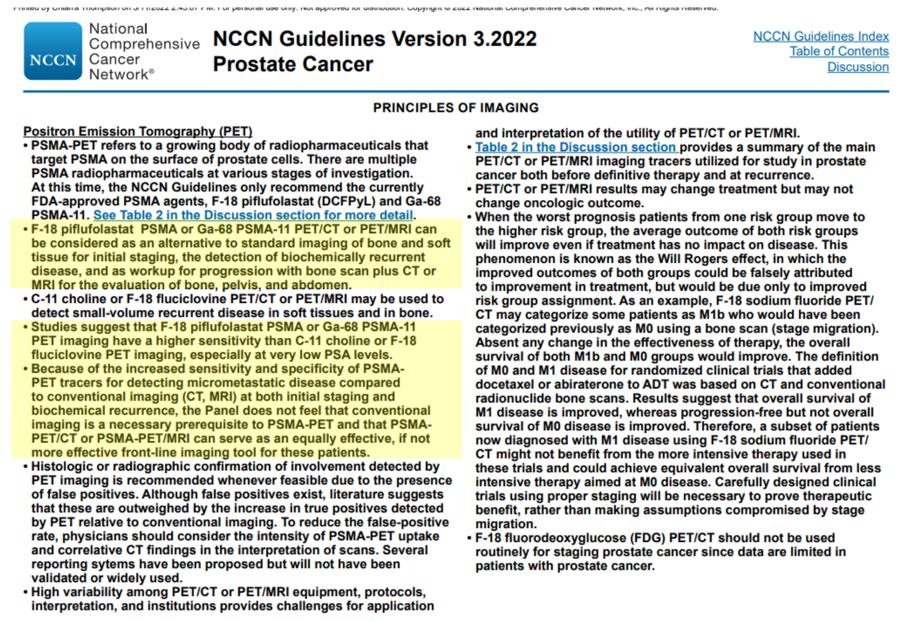
RADIATION THERAPY RECURRENCE



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Prostate Cancer
PRINCIPLES OF IMAGING

- Histologic or radiographic confirmation of involvement detected by PET imaging is recommended whenever feasible due to the presence of false positives. Although false positives exist, literature suggests that these are outweighed by the increase in true positives detected by PET relative to conventional imaging. To reduce the false-positive rate, physicians should consider the intensity of PSMA-PET uptake and correlative CT findings in the interpretation of scans. Several reporting sytems have been proposed but will not have been validated or widely used.
- High variability among PET/CT or PET/MRI equipment, protocols, interpretation, and institutions provides challenges for application

CT might not benefit from the more intensive therapy used in these trials and could achieve equivalent overall survival from less intensive therapy aimed at M0 disease. Carefully designed clinical trials using proper staging will be necessary to prove therapeutic benefit, rather than making assumptions compromised by stage migration.

- F-18 fluorodeoxyglucose (FDG) PET/CT should not be used routinely for staging prostate cancer since data are limited in patients with prostate cancer.

Appropriate Use Criteria

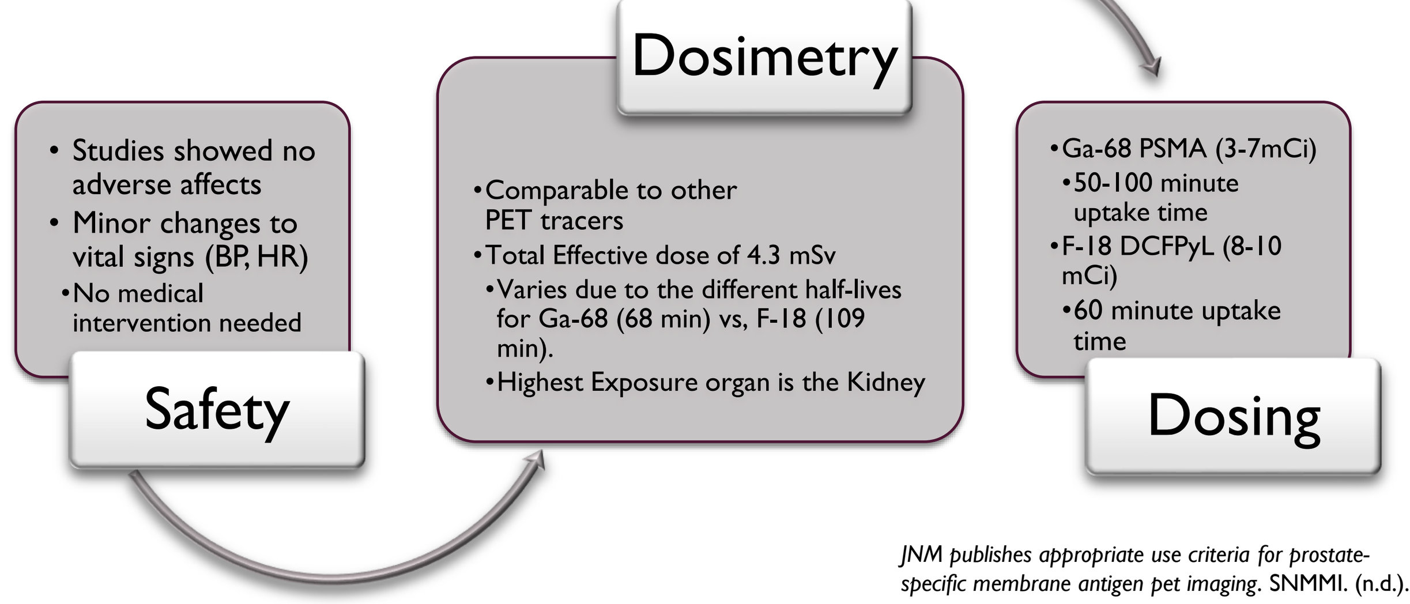
Clinical Scenarios for Prostate Cancer

Scenario #	Description	Appropriateness	Score
1	Patients with suspected prostate cancer (e.g., high/rising PSA levels, abnormal digital rectal examination results) evaluated for targeted biopsy and detection of intraprostatic tumor	Rarely Appropriate	3
2	Patients with very low, low, and favorable intermediate-risk prostate cancer	Rarely Appropriate	2
3	Newly diagnosed unfavorable intermediate, high-risk, or very high-risk prostate cancer	Appropriate	8
4	Newly diagnosed unfavorable intermediate, high-risk, or very high-risk prostate cancer with negative/equivocal or oligometastatic disease on conventional imaging	Appropriate	8
5	Newly diagnosed prostate cancer with widespread metastatic disease on conventional imaging	May be Appropriate	4
6	PSA persistence or PSA rise from undetectable level after radical prostatectomy	Appropriate	9
7	PSA rise above nadir after definitive radiotherapy	Appropriate	9
8	PSA rise after focal therapy of the primary tumor	May be Appropriate	5
9	nmCRPC (M0) on conventional imaging	Appropriate	7
10	Post-treatment PSA rise in the mCRPC setting	May be Appropriate	6
11	Evaluation of response to therapy	May be Appropriate	5

PSMA PET/CT PROTOCOL EXAMPLE (F18-DCFPYL; GA68-PSMA

- **Examinations time:**
  - Uptake Phase: 60 min (Improved lesion characterization may be possible with a second delayed, post void imaging acquisition through the pelvis)
  - Image Acquisition mid-thigh to skull vertex: 10-15 min
  - Image Acquisition whole body:15 -30 min
- **Patient Prep:** None; Hydrate to reduce radiation dose
- **Equipment:** Most advanced available PET Imaging equipment; Greater lesion detectability is likely with time of flight digital imaging using large field of view
- **Radiopharmaceutical**- Either can be used interchangeably
  - F18-DCFPyL Dose: 9 mCi (333 MBq) with an acceptable range of 8 mCi to 10 mCi (296 MBq to 370 MBq)
  - Ga68-PSMA Dose: 3 mCi (111 MBq) to 7 mCi (259 MBq) range
- **Acquisition**
  - Begin 3D image acquisition 60 minutes following injection of the radiotracer
  - PET imaging starts from mid-thigh and proceeds cranially to skull vertex
  - Imaging times per bed for Emission Data Acquisition:
    2-3 minutes per bed position for F18-DCFPyL*
    2-3 minutes per bed position for Ga68-PSMA*
    ** Scanner dependent*

PSMA SAFETY, DOSIMETRY AND DOSE

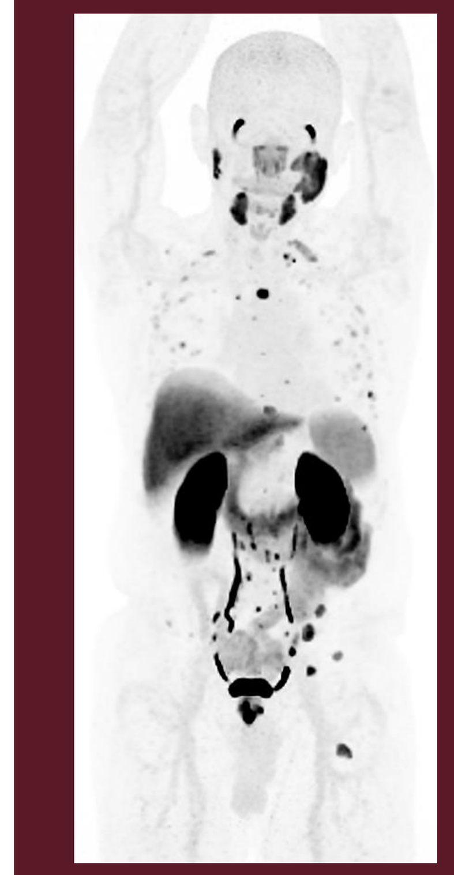

Safety
Studies showed no adverse affects
Minor changes to vital signs (BP, HR)
No medical intervention needed
Dosimetry
Comparable to other PET tracers
Total Effective dose of 4.3 mSv
Varies due to the different half-lives for Ga-68 (68 min) vs, F-18 (109 min).
Highest Exposure organ is the Kidney
Dosing
Ga-68 PSMA (3-7mCi)
50-100 minute uptake time
F-18 DCFPyL (8-10 mCi)
60 minute uptake time

JNM publishes appropriate use criteria for prostate-specific membrane antigen pet imaging. SNMMI. (n.d.).

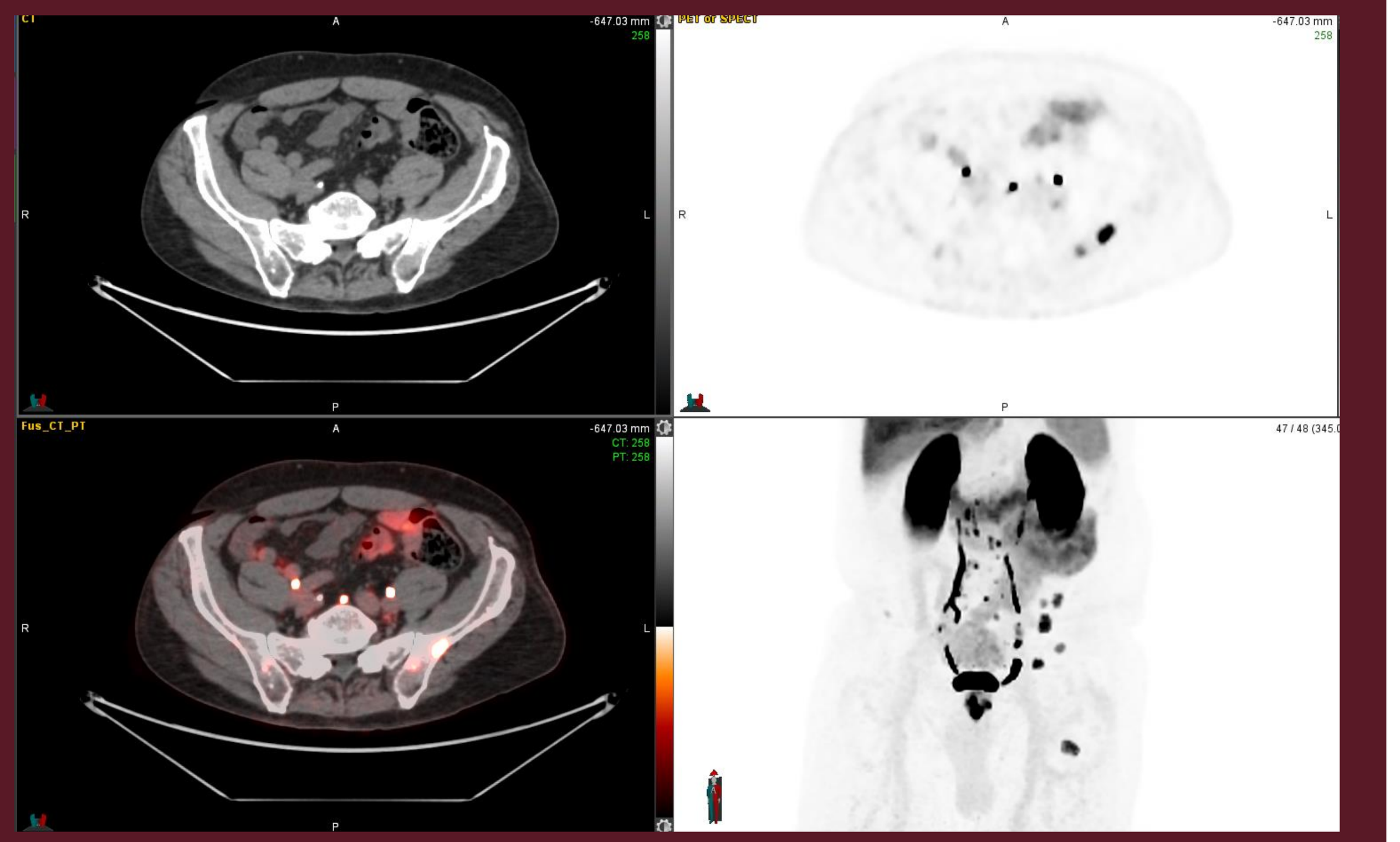
PET IMAGING FOR PROSTRATE CANCER

F-18 FDG	C-11 Choline	F-18 Fluciclovine (Axumin)	PSMA
• Most widely used radiotracer in PET imaging • Compound of radioactive fluorine and glucose	• Accumulates in tissues with high cell proliferation (high rate of cell replication)	• Synthetic amino acid that accumulates in cancerous prostate cells	• Prostate-Specific Membrane Antigen • Peptide radiotracer that binds to the extracellular portion of the PSMA
• Accumulates in tissue with high metabolic activity, such as the brain • Aggressive prostate cancer accumulates high levels of FDG due to rapid cell growth	• Malignancies have higher choline uptake into their cellular membranes	• Prostate cancer cells require a much higher nutrient intake compared to normal tissue, and amino acids are essential for cell metabolism and growth	• Commonly Ga-68 PSMA-11 or F-18 PSMA-DCFPyL • Higher accumulation of the PSMA tracer in cancerous prostate cells compared to healthy cells
• Not the first choice in diagnosis • Used in patients with high grade prostate cancer to determine if there is metastasis to pelvic lymph nodes or the skeleton	• Used in patients with patients with a previous treatment for prostate cancer and increased PSA levels (recurrent prostate cancer) • **Not available for commercial distribution in the U.S.**	• Used in patients with patients with a previous treatment for prostate cancer and increased PSA levels (recurrent prostate cancer) • Widely used for localization of recurrent tumors	• Can be used in patients with newly diagnosed prostate cancer and in patients with suspected recurrent prostate cancer

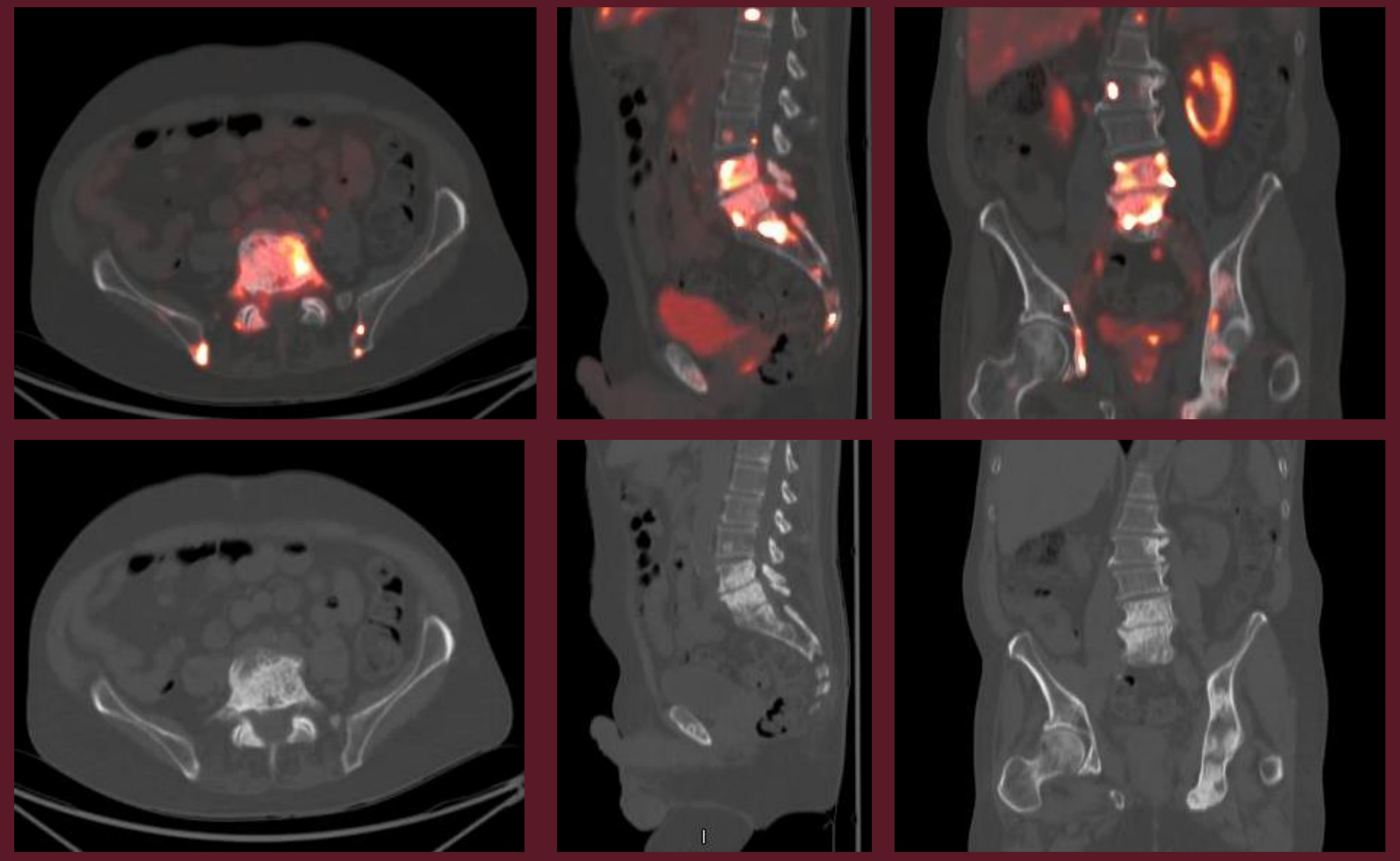
- *Fact sheet: Molecular imaging and prostate cancer*. SNMMI. (n.d.). Retrieved March 6, 2022, from https://www.snmmi.org/AboutSNMMI/Content.aspx?ItemNumber=5662



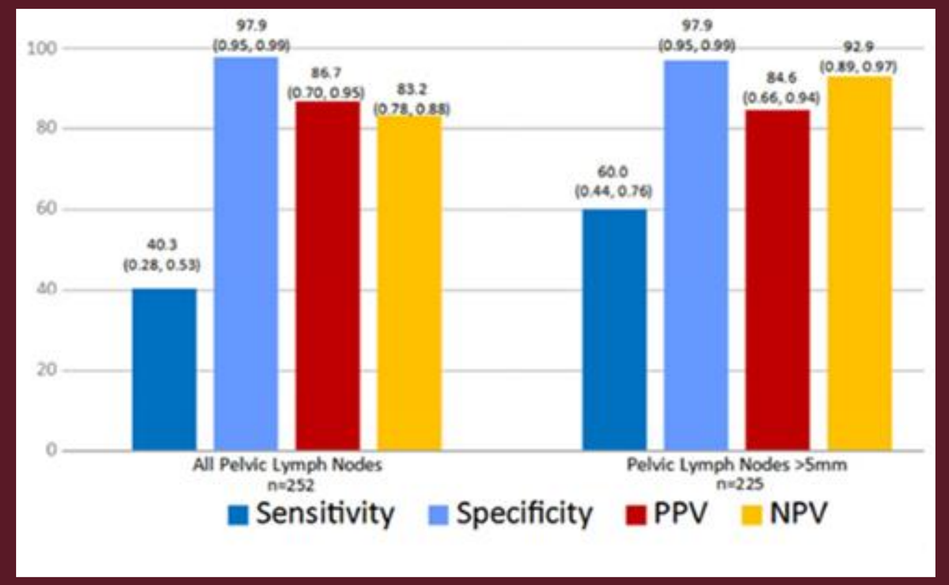
73 year old male with history of prostatic adenocarcinoma status post brachytherapy with PSA of 17.3 ng/mL concerning for prostate cancer recurrence. PSMA PET Maximum Intensity Projection Images demonstrates diffuse tracer avid disease.



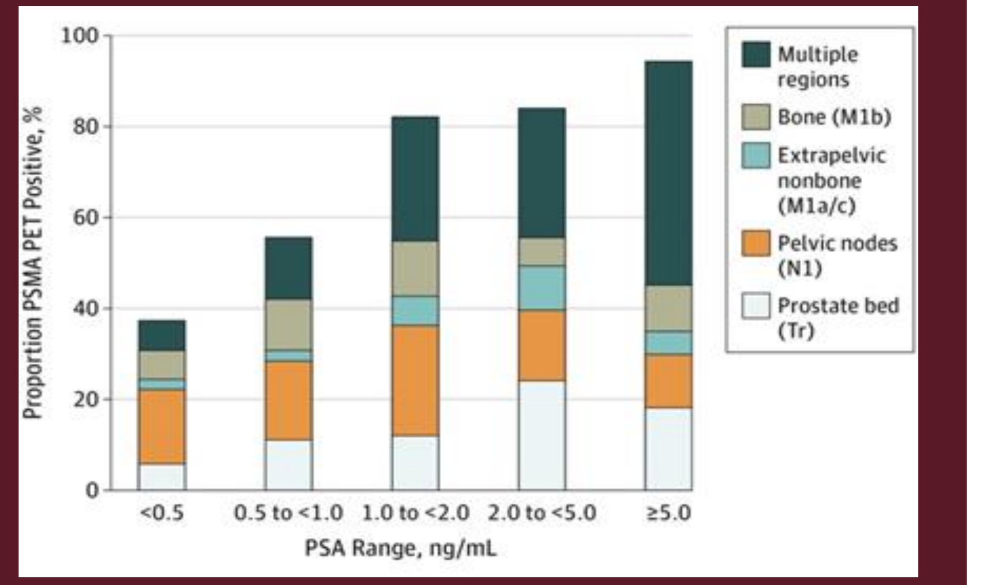
PSMA PET Imaging demonstrates tracer avid subcentimeter presacral/common iliac lymph node measuring approximately 2-3mm with SUV max of 21.9. 5-Ring Digital Time of Flight PET/CT scanner was used which may result in improved millimetric lesion detection.



PSMA PET Imaging demonstrates multiple sclerotic lesions with varying degrees of tracer avidity reflecting both active osseous metastatic disease and nontracer avid treated metastatic lesions.



The OSPREY Trial used a 5mm threshold lymph node size for diagnostic accuracy. The current utilization of Digital Time of Flight PET/CT Scanners allows detection of smaller lesions ranging from 2-3mm.



PSA > or =5: PSMA PET + 97%
PSA >1: PSMA PET + 82%
PSA > 0.5: PSMA PET + 38%

FUTURE OF PSMA - THERANOSTICS

Radioligand Therapy (RLT) using Lu-177 PSMA-617

- Therapeutic radiopharmaceutical delivering beta radiation to specific cell that have high expression of PSMA.
- Similar to the Ga-68/F-18 PSMA radiopharmaceuticals we discussed
  - Lu-177 PSMA-617 binds to the extracellular space in the PSMA structure
  - Therapeutic administration of Lu-177 PSMA would occur following diagnostic evaluation of disease avidity using Ga-68/F-18 PSMA (Theranostic)

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Acknowledgement: I would like to thank Ms. Nancy Gray for her creativity and expertise in the design of this poster.