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Harshad R. Kulkarni and Abass Alavi

Prostate-Specific Membrane Antigen-Based PET Brings New Insights into the Management of Prostate Cancer 555

Cong Hu, Liang Dong, Wei Xue, and Kenneth J. Pienta

Prostate cancer (PCa) is the third most common cancer diagnosed in the world. Since its first identification in 1987 and its first molecular cloning in 1993, prostate-specific membrane antigen (PSMA) has been developed as a theragnostic imaging biomarker and therapeutic agent for PCa. For metastatic castration-resistant PCa, PSMA-based PET imaging can be applied to the monitoring of disease and response assessment with PSMA-based therapeutics. This novel imaging modality is bringing new insights into diagnosis, stratification, and clinical decision-making and treatment.

Role of MRI, Ultrasound, and Computed Tomography in the Management of Prostate Cancer 565

Nancy Mohsen

Computed tomography (CT), MRI, and Ultrasound play an evolving role in prostate cancer management. Multi-parametric MRI has high sensitivity and negative predictive value in prostate cancer diagnosis, leading to increased utilization as part of an active surveillance paradigm in low-to-intermediate-risk patients, and local tumor staging in high-grade cancers. CT is modestly sensitive in staging high-grade tumors to evaluate for nodal, liver, lung, and bone metastasis, and is preferred for assessing treatment related complications. Until recently, ultrasound has been limited to a guidance modality for biopsy and treatment; however, advances in micro-ultrasound technology aim to expand its role diagnosing and managing prostate cancer.

^{18}F-Labeled Radiotracers for Prostate-specific Membrane Antigen: Historical Perspective and Future Directions 585

Steven P. Rowe, Ali Salavati, Rudolf A. Werner, Kenneth J. Pienta, Michael A. Gorin, Martin G. Pomper, and Lilja B. Solnes

Much of the modern growth in nuclear medicine has been driven by PET imaging of prostate-specific membrane antigen (PSMA) in men with prostate cancer. Fluorine-18 is the ideal PET radionuclide with a moderately long half-life, high positron yield, low positron energy, and cyclotron-based production. ^{18}F-DCFPyL is the first Food and Drug Administration-approved compound in this class. In this review, we cover a number of aspects of radiofluorinated PSMA PET agents, including their historical development, the early clinical trials, key multicenter registration trials, emerging clinical agents, new compounds that are entering human use, and future directions for the field.

Ga-68 Prostate-Specific Membrane Antigen PET/CT: Imaging and Clinical Perspective in Prostate Cancer: Imaging and Clinical Perspective in Prostate Cancer 595

Ameya D. Puranik and Indraja D. Dev

Imaging in prostate cancer has become increasingly important over time, as the incidence of prostate cancer has been on the rise and better screening techniques have emerged. The development of personalized systemic therapies highlights the unmet need for whole-body imaging. Prostate-specific membrane antigen (PSMA) PET, with its ease of performance and mechanism of localization to prostatic tumor cells, has now emerged as a preferred modality for diagnosis, staging, and treatment response assessment. In this context, PSMA PET can help in mapping the disease extent, both the skeletal and visceral spread, to plan targeted therapeutic approaches.

Prostate Cancer Imaging with 18F-Fluciclovine 607

Bital Savir-Baruch and David M. Schuster

18F-Fluciclovine PET is approved for the evaluation of patients with suspected prostate cancer recurrence. 18F-Fluciclovine PET is highly specific for the localization of extraprostatic disease even with negative conventional images and low prostate-specific antigen and has been reported to influence patients' management and improve outcome. With the recent Food and Drug Administration approval of prostate-specific membrane antigen (PSMA) PET, 18F-Fluciclovine is likely to be used as an adjunct modality in patients with suspected occult local recurrence and/or negative PSMA findings.

PET Imaging Using Gallium-68 (^{68}Ga) RM2 621

Heying Duan and Andrei Iagaru

Molecular imaging is advancing rapidly with promising new molecular targets emerging for theragnostic, ie, imaging and treatment with the same compound, to provide targeted, personalized medicine. Gastrin-releasing peptide receptors (GRPR) are overexpressed in prostate cancer. Gallium-68 (68Ga) RM2 is a GRPR antagonist and shows high sensitivity and specificity for the detection of primary prostate cancer and recurrent disease. However, compared with the widely used 68Ga-PSMA11 and 18F-DCFPyL, a discordance in uptake pattern is seen reflecting the heterogeneity in tumor biology of prostate cancer. In this review, we present the background, current status, and future perspectives of PET imaging using 68Ga-RM2.

Feasibility of Global Assessment of Bone Metastases in Prostate Cancer with ^{18}F-Sodium Fluoride-PET/Computed Tomography 631

Benjamin Koa, William Y. Raynor, Peter Sang Uk Park, Austin J. Borja, Sachi Singhal, Angie Kuang, Vincent Zhang, Thomas J. Werner, Abass Alavi, and Mona-Elisabeth Revheim

18F-sodium fluoride (NaF) PET/computed tomography (CT) allows detection of bone metastases in patients with prostate cancer (PCa). The aim of this study was to test the feasibility of assessing global metastatic bone disease in patients with PCa by using a threshold-based PET segmentation technique. This retrospective analysis was performed in 32 patients with PCa with known bone metastases who underwent NaF-PET/CT imaging. An adaptive contrast-oriented thresholding technique was used to segment NaF avid lesions. The mean metabolic volumetric product (MVPmean), partial volume-corrected MVPmean (cMVPmean), and metabolically

active volume (MAV) were calculated. Lesional values were summed within each patient to obtain the global PET disease burden. Pearson correlation analysis was used to assess the associations between global NaF-PET/CT metrics and clinical biomarkers of metastatic disease activity. Global MVPmean, cMVPmean, and MAV were significantly correlated with alkaline phosphatase (ALP) levels ($p < 0.05$). No correlation was observed between global NaF-PET/CT measures and prostate-specific antigen (PSA) levels. Global assessment is a feasible method to quantify metastatic bone disease activity in patients with PCa. Convergent validity was supported by demonstrating a significant correlation between NaF-PET/CT parameters and blood ALP levels.

Dual-Tracer PET-Computed Tomography Imaging for Precision Radio-Molecular Theranostics of Prostate Cancer: A Futuristic Perspective **641**

Aadil Adnan and Sandip Basu

Dual/multi-tracer PET-computed tomography (CT) scan has been an interesting and intriguing concept and is promising in noninvasive and overall characterization of tumor biology and heterogeneity and has scientifically augmented the practice of precision oncology. In prostate carcinoma, particularly in metastatic castration-resistant prostate carcinoma setting, dual-tracer PET-CT can be potentially useful in selecting patients for chemotherapy, androgen deprivation therapy or prostate-specific membrane antigen (PSMA)-based peptide receptor radioligand therapy either as mono-therapy or as combination therapy, ascertaining differentiation status, staging/restaging, prognostication, and predicting progression/response. PSMA PET/CT has great potential as a "rule out" test in baseline staging, while being very useful in restaging and metastatic workup.

Assessing Coronary Artery and Aortic Calcification in Patients with Prostate Cancer Using ^{18}F-Sodium Fluoride PET/Computed Tomography **653**

William Y. Raynor, Austin J. Borja, Vincent Zhang, Esha Kothekar, Hui Chong Lau, Sze Jia Ng, Siavash Mehdizadeh Seraj, Chaitanya Rojulpote, Raheleh Taghvaei, Kevin Yu Jin, Thomas J. Werner, Poul Flemming Høilund-Carlsen, Abass Alavi, and Mona-Elisabeth Revheim

The aim of this study was to assess coronary artery and aortic calcification in healthy controls, angina pectoris patients, and prostate cancer patients using 18F-sodium fluoride PET/computed tomography (NaF-PET/CT). A retrospective analysis compared 33 prostate cancer patients with 33 healthy subjects and 33 patients with angina pectoris. Increased target-to-background ratio (TBR) of the coronary arteries, ascending aorta, aortic arch, and descending aorta was observed in cancer patients compared to healthy controls but not compared to angina pectoris patients. These results demonstrate the feasibility of assessing vascular microcalcification with NaF-PET/CT, with significant differences in uptake according to comorbidities.