Case series – ^{18}F-DCFPyL-positron emission tomography/computed tomography (PET/CT) time of imaging

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Introduction

Prostate cancer is the most commonly diagnosed cancer, except for skin cancer, and the second leading cause of cancer-related death among Canadian males.[1] Recurrence is not uncommon, despite local therapies, such as radical prostatectomy, radiation, brachytherapy, and systemic therapies, including hormonal therapy.[2] Often, the first sign of recurrence is a rising prostate-specific antigen (PSA), known as "biochemical recurrence."[3] Based on the European Association of Urology and American Urological Association guidelines, biochemical recurrence is defined as serum PSA value of ≥0.2 ng/ml after prostatectomy and ≥2 ng/ml increase above the nadir PSA after external beam radiation therapy of the primary tumor.[3] In recent years, prostate-specific membrane antigen targeted positron emission tomography/computed tomography (PSMA-PET/CT) has revolutionized the detection of disease in men with biochemical recurrence and has led to a change in management.[4]

^{68}Ga-PSMA-11 is arguably the most widely used PET radiopharmaceutical worldwide for the detection of prostate cancer. However, it has limitations, such as a short physical half-life (68 minutes). ^{18}F-labeled PSMA-targeting radiopharmaceuticals are easier to distribute, given their longer half-life (110 minutes). ^{18}F-DCFPyL is the most commonly used ^{18}F-labeled PSMA-targeting radiopharmaceutical in Canada. The biodistribution patterns of ^{68}Ga-PSMA and ^{18}F-DCFPyL are similar.[5] Many centers acquire images 60 minutes post-intravenous administration of ^{18}F-DCFPyL. In this paper, we illustrate the value of dual-time point imaging and compare the imaging at 60 and 120 minutes post-radiopharmaceutical injection. All cases had biochemical recurrence with negative bone and CT scans.

Case 1

A 70-year-old male with biochemically recurrent prostate cancer (PSA 0.3 ng/mL) was referred for PSMA-PET/CT. He was treated with radical prostatectomy and hormonal therapy 10 years ago but has been off hormonal therapy for two years. Total body images obtained 60 minutes following intraveous^{18}F-DCFPyL administration showed intense focal radiopharmaceutical uptake in a left internal iliac lymph node and mild focal uptake in para-aortic soft tissue to the left of the aortic bifurcation (Fig. 1A). Additional imaging of the pelvis performed 120 minutes post-radiopharmaceutical injection showed an interval increase uptake in the left internal iliac lymph node consistent with prostate cancer spread and an interval decrease in uptake in the para-aortic soft tissue consistent with the organ of Zuckerkandl (Fig. 1B). Radiopharmaceutical uptake in the sympathetic ganglia and organ of Zuckerkandl can be mistaken for malignant disease spread and is a known pitfall of PSMA-PET/CT.[6] In addition to the lesion location and shape, an interval reduction in conspicuity on delayed images suggests a benign process, while an interval increase in conspicuity suggests malignant disease spread.[6,7] This case illustrates the value of dual time-point ^{18}F-DCFPyL PET/CT, similar to multiphase ^{68}Ga-PSMA PET/CT.[8] In this case, the staging could have been potentially changed, as the internal iliac node (the shown avid node) is a locoregional node for prostate cancer, but a node at the level of aortic bifurcation is considered metastatic.

Case 2

A 69-year-old male with biochemically recurrent prostate cancer (PSA 10.9 ng/mL) three years post-external radiation therapy was referred for PSMA-PET/CT. The images obtained 60 min-

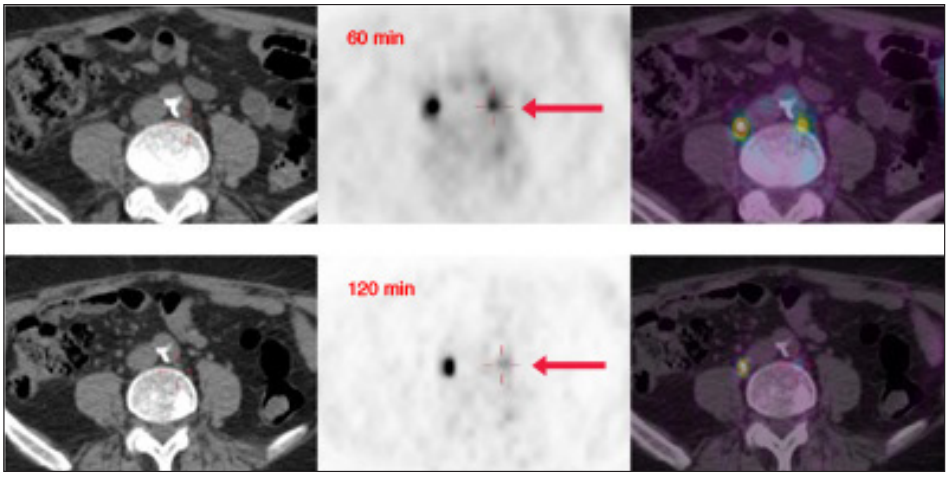

Fig. 1A. Case 1: Total body images obtained 60 minutes following intraveous^{18}F-DCFPyL administration showed intense focal radiopharmaceutical uptake in a left internal iliac lymph node and mild focal uptake in para-aortic soft tissue to the left of the aortic bifurcation.

utes following intravenous ^{18}F-DCFPyL administration showed equivocal mild focal uptake in a prevertebral soft tissue nodule (Fig. 2A). Interval increase in the radiopharmaceutical uptake on delayed images obtained 120 minutes following intravenous ^{18}F-DCFPyL administration, however, was consistent with prostate cancer spread to a small pre-sacral lymph node (Fig. 2B). Given high PSA at biochemical recurrence, hormone therapy was started. Also, the patient was offered regional pelvic radiation therapy, given the positive PSMA PET/CT finding. His PSA dropped to 1.02 ng/mL post-treatment.

Case 3

A 77-year-old male with history of Gleason 4+3 prostate adenocarcinoma developed biochemically recurrent prostate cancer eight years post-radical prostatectomy (PSA 1.7 ng/mL) and subsequently was referred for PSMA-PET/CT. The images obtained 60 minutes following radiopharmaceutical administration showed intense focal radiopharmaceutical uptake in the prostate bed without a suspicious correlating anatomic abnormality, suspicious for prostate cancer. Indeed, the retro-vesical region or prostate bed is a common site of local recurrence.[9] However, this radiopharmaceutical activity resolved on 120-minute images, consistent with physiological activity in the genitourinary tract (Figs. 3A, 3B). In addition, a mildly ^{18}F-DCFPyL-avid right obturator node, which may have been missed on early imaging (SUVmax 1.7), showed increasing conspicuity on delayed imaging (SUVmax 2.6) consistent with malignant disease spread. The patient underwent external beam radiation of a single node detected on delayed imaging and his PSA became undetectable.

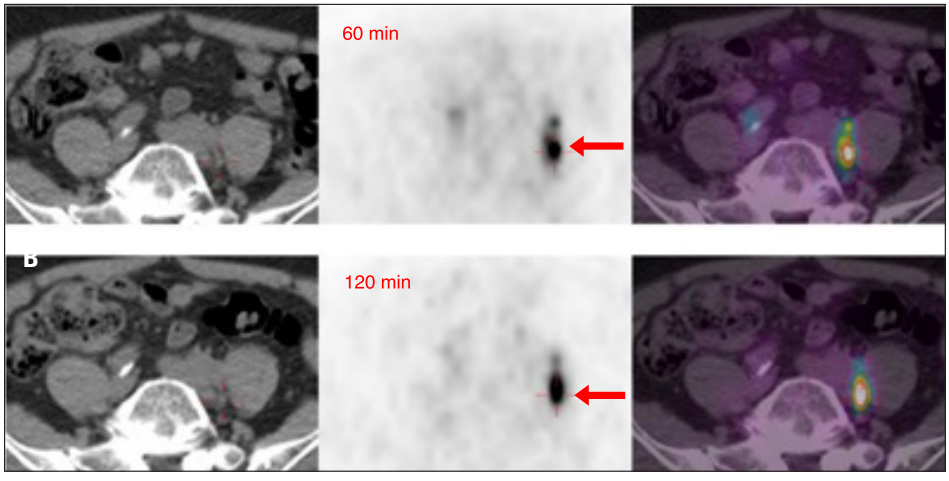

Fig. 1B. Case 1: Additional imaging of the pelvis performed 120 minutes post-radiopharmaceutical injection showed an interval increase uptake in the left internal iliac lymph node consistent with prostate cancer spread and an interval decrease in uptake in the para-aortic soft tissue consistent with the organ of Zuckerkandl.

Case 4

A 62-year-old male with biochemically recurrent prostate cancer adenocarcinoma 14 years post-radical prostatectomy (PSA 1.3 ng/mL) was referred for PSMA-PET/CT. Focal intense radiopharmaceutical uptake in a small peri-ureteric left external iliac lymph node on images obtained 60 minutes following radiopharmaceutical administration increased in conspicuity at 120 minutes, consistent with prostate cancer spread. On the other hand, focal uptake in the right peri-ureteric region on images obtained 60 minutes following radiopharmaceutical administration resolved at 120 minutes, consistent with physiological activity in the genitourinary tract (Fig. 4). Repeat delayed imaging in cases of urine activity is helpful to avoid upstaging or downstaging cases.

Discussion

While the ratio of target-to-background radiopharmaceutical uptake on PSMA-targeted PET/CT typically decreases over time in benign and physiological processes, it increases in malignant disease, making dual time-point imaging helpful.[10,11] As

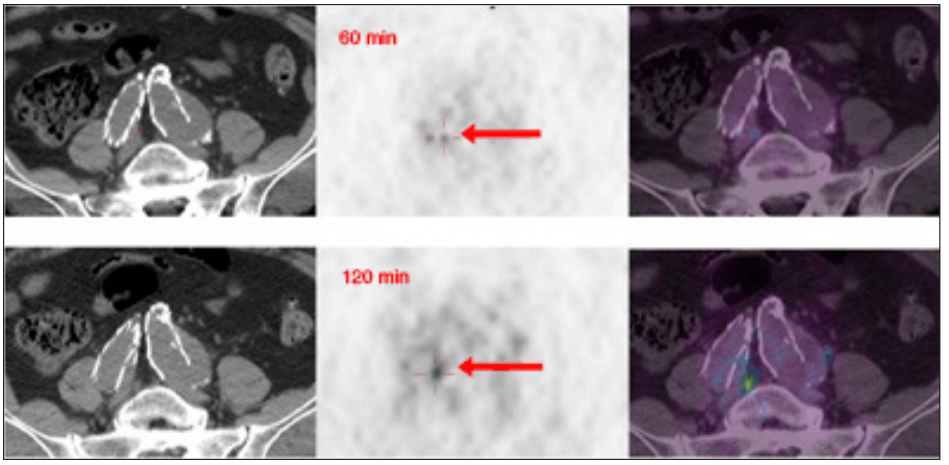

Fig. 2. (A) The images obtained 60 minutes following intravenous ^{18}F-DCFPyL administration showed an equivocal mild focal uptake in a prevertebral soft tissue nodule. ***(B)*** Interval increase in the radiopharmaceutical uptake on delayed images obtained 120 minutes following intravenous ^{18}F-DCFPyL administration, however, was consistent with prostate cancer spread to a small pre-sacral lymph node.

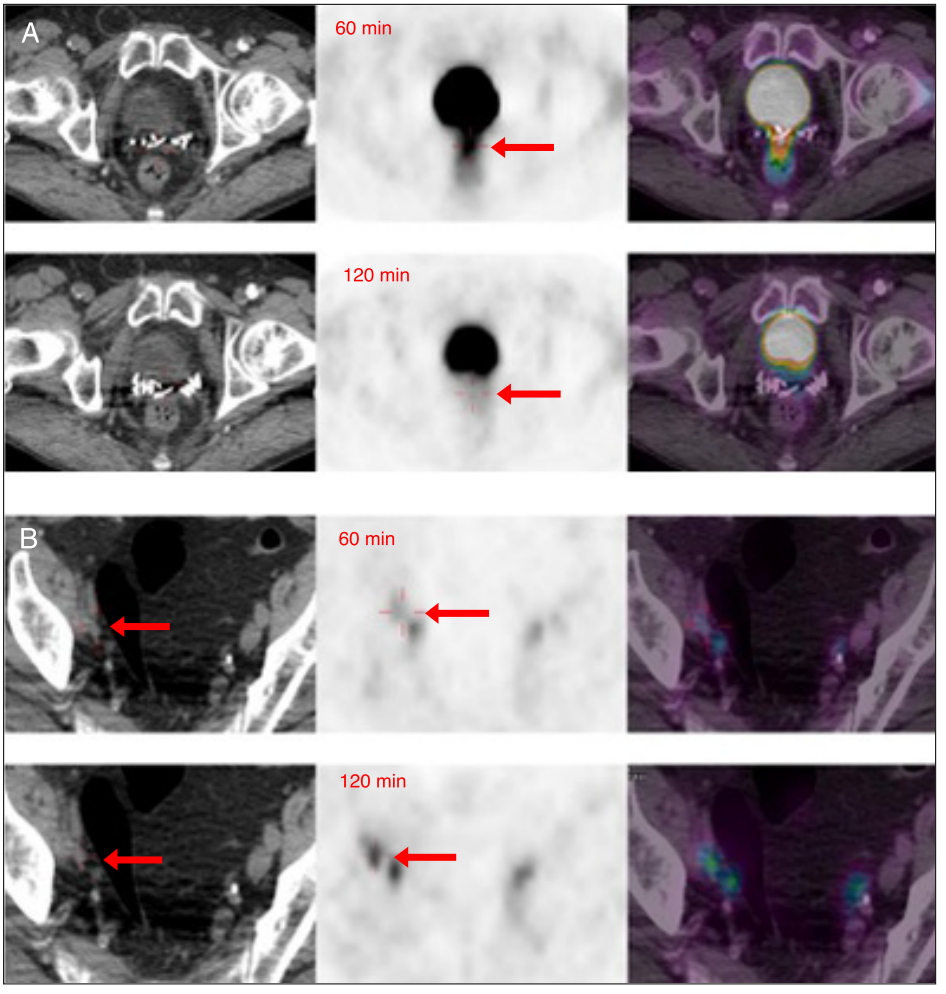

Fig. 3. Case 3: (A) The images obtained 60 minutes following radiopharmaceutical administration showed intense focal radiopharmaceutical uptake in the prostate bed without a suspicious correlating anatomic abnormality, suspicious for prostate cancer. ***(B)*** However, this radiopharmaceutical activity resolved on 120 minutes images consistent with physiological activity in the genitourinary tract.

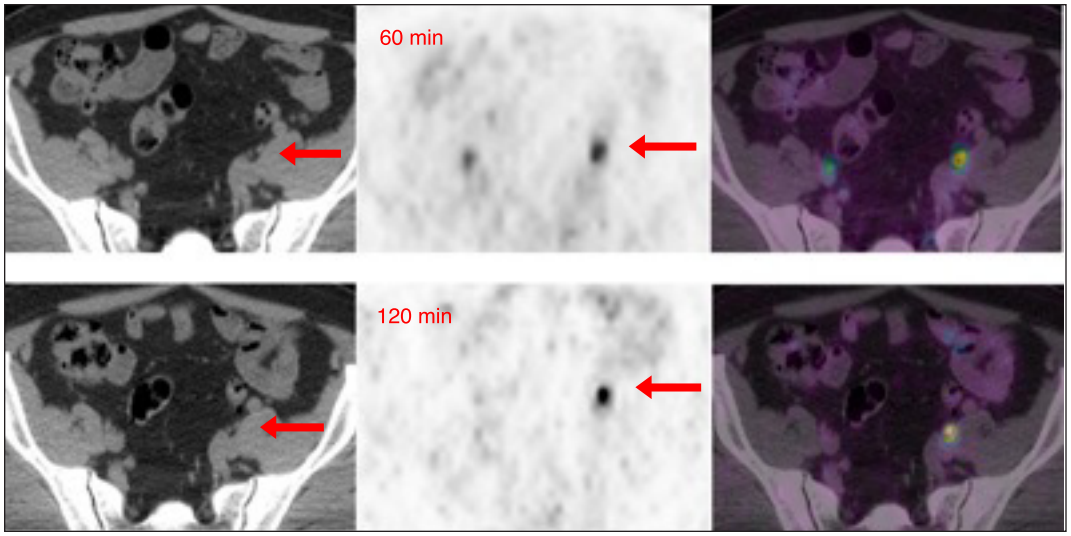

Fig. 4. Case 4: Focal intense radiopharmaceutical uptake in a small peri-ureteric left external iliac lymph node on images obtained 60 minutes following radiopharmaceutical administration, increased in conspicuity at 120 minutes consistent with prostate cancer spread.

illustrated above, benign uptake, such as ganglion uptake and urine activity, were reduced and cleared on delayed images, while involved nodes showed interval increase in conspicuity. Unfortunately, practical considerations, including workflow issues and patient preference, may limit the implementation of dual time-point imaging in clinical practice.[7] Given issues of accessibility, dual time-point imaging could be reserved for characterization of equivocal findings. While checking individual cases prior to a patient leaving the department may be an option for centers with low PSMA-PET/CT volume, ultimately, if a choice must be made to perform either early or late imaging, an uptake time of 120 minutes is preferred.[10] This is true regardless of whether the radiopharmaceutical used for PSMA-targeted PET is labeled with gallium-68 or fluoride-18.[10-14]

Competing interests: The authors do not report any competing personal or financial interests related to this work.

This paper has been peer-reviewed.

References

1. Brenner DR, Weir HK, Demers AA, et al. Projected estimates of cancer in Canada in 2020. *CMAJ* 2020;192:199-205. https://doi.org/10.1503/cmaj.191292
2. So AI, Chi KN, Danielson B, et al. Canadian Urological Association-Canadian Urologic Oncology Group guideline on metastatic castration-naive and castration-sensitive prostate cancer. *Can Urol Assoc J* 2020;14:17-23. https://doi.org/10.5489/cuaj.6384
3. Gillessen S, Attard G, Beer TM, et al. Management of patients with advanced prostate cancer: Report of the Advanced Prostate Cancer Consensus Conference 2019. *Eur Urol* 2020;77:508-47. https://doi.org/10.1016/j.eururo.2020.01.012
4. Perera M, Papa N, Roberts M, et al. Gallium-68 prostate-specific membrane antigen positron emission tomography in advanced prostate cancer-updated diagnostic utility, sensitivity, specificity, and distribution of prostate-specific membrane antigen-avid lesions: A systematic review and meta-analysis. *Eur Urol* 2020;77:403-17. https://doi.org/10.1016/j.eururo.2019.01.049
5. Ferreira G, Iravani A, Hofman MS, et al. Intra-individual comparison of ^{68}Ga-PSMA-11 and ^{18}F-DCFPyL normal-organ biodistribution. *Cancer Imag* 2019;19:23. https://doi.org/10.1186/s40644-019-0211-y
6. Rischpler C, Beck TI, Okamoto S, et al. ^{68}Ga-PSMA-HBED-CC uptake in cervical, celiac, and sacral ganglia as an important pitfall in prostate cancer PET imaging. *J Nucl Med* 2018;59:1406-11. https://doi.org/10.2967/jnumed.117.204677
7. Afshar-Oromieh A, Sattler LP, Steiger K, et al. Tracer uptake in mediastinal and para-aortal thoracic lymph nodes as a potential pitfall in image interpretation of PSMA ligand PET/CT. *Eur J Nucl Med Mol Imaging* 2018;45:1179-87. https://doi.org/10.1007/s00259-018-3965-8
8. Beheshti M, Manafi-Farid R, Geinitz H, et al. Multiphasic ^{68}Ga-PSMA PET/CT in detection of early recurrence in prostate cancer patients with PSA <1 ng/ml: A prospective study of 135 cases. *J Nucl Med* 2020;61:1484-90. https://doi.org/10.2967/jnumed.119.238071
9. Barbosa FG, Queiroz MA, Nunes RF, et al. Revisiting prostate cancer recurrence with PSMA PET: Atlas of typical and atypical patterns of spread. *Radiographics* 2019;39:186-212. https://doi.org/10.1148/rg.2019180079
10. Wondergem M, van der Zant FM, Knol RJJ, et al. ^{18}F-DCFPyL PET/CT in the detection of prostate cancer at 60 and 120 minutes: Detection rate, image quality, activity kinetics, and biodistribution. *J Nucl Med* 2017;58:1797-1804. https://doi.org/10.2967/jnumed.117.192658
11. Hoffmann MA, Buchholz HG, Wieler HJ, et al. Dual-time point [68Ga] Ga-PSMA-11 PET/CT hybrid imaging for staging and restaging of prostate cancer. *Cancers* 2020;12:2788. https://doi.org/10.3390/cancers12102788
12. Derlin T, Weiberg D, von Klot C, et al. ^{68}Ga-PSMA I&T PET/CT for assessment of prostate cancer: Evaluation of image quality after forced diuresis and delayed imaging. *Eur Radiol* 2016;26:4345-53. https://doi.org/10.1007/s00330-016-4308-4
13. Schmuck S, Nordlohne S, von Klot CA, et al. Comparison of standard and delayed imaging to improve the detection rate of [(68)Ga]PSMA I&T PET/CT in patients with biochemical recurrence or prostate-specific antigen persistence after primary therapy for prostate cancer. *Eur J Nucl Med Mol Imaging* 2017;44:960-8. https://doi.org/10.1007/s00259-017-3669-5
14. Hofman MS, Hicks RJ, Maurer T, et al. Prostate-specific membrane antigen PET: Clinical utility in prostate cancer, normal patterns, pearls, and pitfalls. *Radiographics* 2018;38:200-17. https://doi.org/10.1148/rg.2018170108

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