



18F-PSMA-1007 PET/CT Detects Micrometastases in a Patient With Biochemically Recurrent Prostate Cancer

Frederik L. Giesel,¹ Claudia Kesch,² Mijin Yun,³ Jens Cardinale,⁴ Uwe Haberkorn,¹ Klaus Kopka,⁴ Clemens Kratochwil,¹ Boris A. Hadaschik²

Clinical Practice Points

- To date, several radioactive tracers for imaging primary and recurrent prostate cancer are undergoing active investigation.
- In this case report fluorine-18 (¹⁸F)—prostate-specific membrane antigen (PSMA)-1007 positron emission tomography (PET)/computed tomography imaging was performed, to our knowledge, for the first time in a patient with biochemical recurrence (prostate-specific antigen [PSA] 0.08 µg/L) after radical prostatectomy and adjuvant radiation.
- Seventeen lymph nodes with increased tracer uptake along the retroperitoneum and iliac arteries were detected. Therefore, early treatment with intermittent androgen deprivation was initiated instead of locoregional salvage therapy.
- Hence, ¹⁸F-PSMA-1007 PET imaging at very low PSA levels provided critical information to correctly restage disease.

Clinical Genitourinary Cancer, Vol. 15, No. 3, e497-9 © 2016 The Author(s). Published by Elsevier Inc. This is an open access article

under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Keywords: Biochemical recurrence, Imaging, Positron emission tomography, Radiotracer-labeled prostate-specific membrane antigen, Staging

Introduction

Radiotracer-labeled prostate-specific membrane antigen (PSMA) targeting positron emission tomography (PET) revolutionized prostate cancer imaging. In the following case study we evaluated the new fluorine-18 (¹⁸F)-PSMA-1007 tracer, to our knowledge, for the first time, in a patient with biochemical recurrence.

Case

In August 2016, a 79-year-old man was referred to our clinic, with the request for restaging of prostate cancer because of slowly

rising prostate-specific antigen (PSA) levels 9 years after radical prostatectomy and adjuvant radiotherapy. Technetium 99m-methyl diphosphonate whole body bone scan, computed tomography (CT) and magnetic resonance imaging (MRI) of the abdomen and pelvis revealed no remarkable pathological finding.

In March 2007, the patient was diagnosed with intermediate-risk prostate cancer and prostatectomy was performed, which presented with positive margins (pT3a, N0, M0; Gleason score 4+3; positive margins with tumor infiltration at the apical left site of the prostate). Adjuvant radiotherapy was administered to the prostatic bed with 60 Gy in 30 fractions. The PSA level decreased from 5.3 before to 0.03 ng/mL after surgery. Regular laboratory tests showed a gradual increase of PSA levels up to 0.08 ng/mL in July 2016, suggesting vital tumor tissue somewhere that might be amenable to salvage therapy such as stereotactic body radiation or high-intensity focused ultrasound, if found.

After multidisciplinary discussion we decided to perform PET/CT imaging with the ¹⁸F-labeled PSMA-targeted radioligand PSMA-1007, an experimental molecular PET radiotracer, which has been described to have higher detection rates compared with standard morphological imaging modalities such as CT and MRI.¹

¹Department of Nuclear Medicine

²Department of Urology, University Hospital Heidelberg, Heidelberg, Germany

³Department of Nuclear Medicine, Yonsei University Severance Hospital, Seoul, South Korea

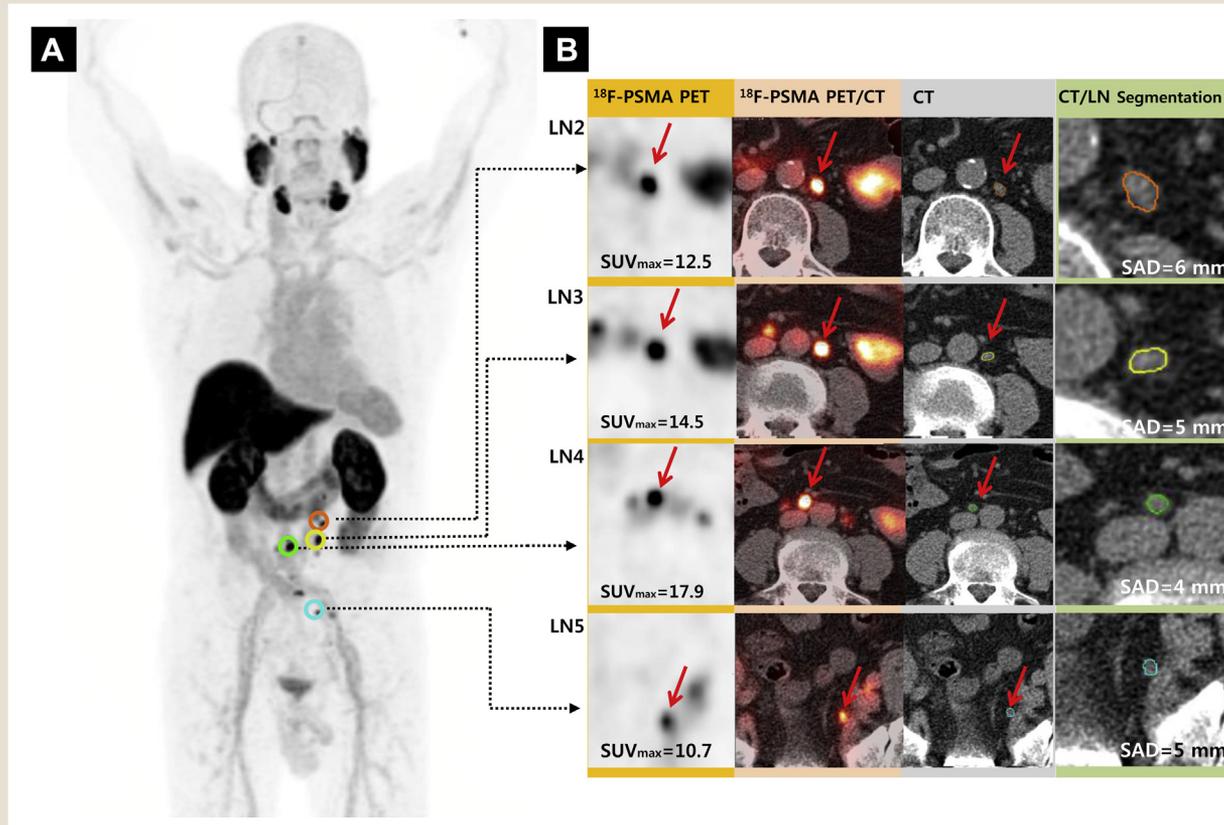
⁴Division of Radiopharmaceutical Chemistry, German Cancer Research Centre, Heidelberg, Germany

Submitted: Dec 13, 2016; Accepted: Dec 22, 2016; Epub: Dec 29, 2016

Address for correspondence: Frederik L. Giesel, MD, Department of Nuclear Medicine, University Hospital Heidelberg, Im Neuenheimer Feld 400, Heidelberg 69120, Germany

Fax: +49-6221-56-8672; e-mail contact: frederik@egiesel.com

Figure 1 (A) Fluorine-18 (^{18}F)-Prostate-Specific Membrane Antigen (PSMA)-1007 Maximum Intensity Projection-Positron Emission Tomography (PET)/Computed Tomography (CT) in a Patient With Biochemical Recurrence After Prostatectomy Presented Lymph Nodes With Increased ^{18}F -PSMA-1007 Uptake, Consistent With Lymph Node Metastases. All ^{18}F -PSMA-1007 Positive Lymph Nodes (B) Were Under CT-Morphological Detection Rate; in Contrast All Lymph Nodes Presented a High PSMA-1007 Uptake in PET



Abbreviation: SUV = standardized uptake value.

The patient underwent ^{18}F -PSMA-1007 PET/CT imaging and, surprisingly, 17 lymph nodes were detected with increased PSMA uptake ($n = 17$; median = standardized uptake value (SUV) $\text{max} = 7.71$; maximum = 18.8/minimum = 3.2) along the retroperitoneum and iliac arteries, which were consistent with prostate cancer recurrence. An automated segmented volumetric analysis was applied to measure the sizes of ^{18}F -PSMA-1007-positive lymph nodes. All were below the morphological detection limit and thus could be not considered as lymph node metastasis according to Response Evaluation Criteria in Solid Tumors criteria ($n = 17$; median = 4.6 mm; maximum = 6.6/minimum = 3.2 mm; Figure 1). Because of ^{18}F -PSMA-1007-positive prostate cancer spread along the lymph nodes, the patient was classified as M1. Therefore, early treatment with intermittent androgen deprivation was initiated instead of locoregional salvage therapy.^{2,3}

Discussion

In patients with biochemical recurrence localization of recurrent prostate cancer is essential for further therapy planning. Conventional

cross-sectional imaging or bone scintigraphy shows only limited detection rates in these cases, especially at low serum PSA values.⁴ Therefore, several radioactive tracers for improved imaging of recurrent but also primary prostate cancer are under active investigation.⁵⁻⁹ PSMA radioligands have been presented so far as the most sensitive and specific with regard to prostate cancer detection, in particular in high-risk prostate cancer patients. For the most commonly used ^{68}Ga -PSMA-11 radioligand, detection rates of 50% to 57.9% are described in patients with biochemical recurrence and serum PSA levels < 0.5 ng/mL.^{10,11} Nevertheless, ^{18}F -PSMA-1007 does have some advantageous characteristics: ^{18}F is produced by a cyclotron facilitating a higher available amount of radioisotope compared with generator-capacity bound ^{68}Ga -PSMA. Its low positron emission energy results in a higher image resolution and its partially hepatobiliary elimination might ease the evaluation of the prostate bed and pelvis.^{12,13} In this case report ^{18}F -PSMA-1007 was used, to our knowledge, for the first time, in a patient with biochemically recurrent prostate cancer and 17 lymph nodes were detected with increased PSMA uptake at a PSA serum level of 0.08 ng/mL implying major potential for staging recurrent prostate cancer.

Conclusion

Novel ¹⁸F-PSMA-1007 PET imaging at very low PSA levels provided critical information to correctly restage disease and to discuss appropriate treatment options.

Acknowledgments

Written informed consent was obtained from the patient.

Disclosure

J.C., F.L.G., U.H., and K.K. disclose a patent application for PSMA-1007. The remaining authors have stated that they have no conflicts of interest.

References

1. Perera M, Papa N, Christidis D, et al. Sensitivity, specificity, and predictors of positive (68)Ga-prostate-specific membrane antigen positron emission tomography in advanced prostate cancer: a systematic review and meta-analysis. *Eur Urol* 2016; 70:926-37.
2. Carrie C, Hasbini A, de Laroche G, et al. Salvage radiotherapy with or without short-term hormone therapy for rising prostate-specific antigen concentration after radical prostatectomy (GETUG-AFU 16): a randomised, multicentre, open-label phase 3 trial. *Lancet Oncol* 2016; 17:747-56.
3. Crook JM, O'Callaghan CJ, Duncan G, et al. Intermittent androgen suppression for rising PSA level after radiotherapy. *N Engl J Med* 2012; 367:895-903.
4. Rouvière O, Vitry T, Lyonnet D. Imaging of prostate cancer local recurrences: why and how? *Eur Radiol* 2010; 20:1254-66.
5. Haberkorn U, Eder M, Kopka K, Babich JW, Eisenhut M. New strategies in prostate cancer: prostate-specific membrane antigen (PSMA) ligands for diagnosis and therapy. *Clin Cancer Res* 2016; 22:9-15.
6. Haberkorn U, Kopka K, Hadaschik B. Positron emission tomography—computed tomography with prostate-specific membrane antigen ligands as a promising tool for imaging of prostate cancer. *Eur Urol* 2016; 69:397-9.
7. Kiess AP, Banerjee SR, Mease RC, et al. Prostate-specific membrane antigen as a target for cancer imaging and therapy. *Q J Nucl Med Mol Imaging* 2015; 59: 241-68.
8. Kratochwil C, Afshar-Oromieh A, Kopka K, Haberkorn U, Giesel FL. Current status of prostate-specific membrane antigen targeting in nuclear medicine: clinical translation of chelator containing prostate-specific membrane antigen ligands into diagnostics and therapy for prostate cancer. *Semin Nucl Med* 2016; 46:405-18.
9. Rowe SP, Gorin MA, Allaf ME, et al. PET imaging of prostate-specific membrane antigen in prostate cancer: current state of the art and future challenges. *Prostate Cancer Prostatic Dis* 2016; 19:223-30.
10. Afshar-Oromieh A, Malcher A, Eder M, et al. PET imaging with a [68Ga]gallium-labelled PSMA ligand for the diagnosis of prostate cancer: biodistribution in humans and first evaluation of tumour lesions. *Eur J Nucl Med Mol Imaging* 2013; 40:486-95.
11. Eiber M, Maurer T, Souvatzoglou M, et al. Evaluation of Hybrid 68Ga-PSMA ligand PET/CT in 248 patients with biochemical recurrence after radical prostatectomy. *J Nucl Med* 2015; 56:668-74.
12. Cardinale J, Schäfer M, Benešová M, et al. Preclinical evaluation of [18F]PSMA-1007: a new PSMA-ligand for prostate cancer imaging. *J Nucl Med*, Published online October 27, 2016; <http://dx.doi.org/10.2967/jnumed.116.181768>.
13. Giesel FL, Hadaschik B, Cardinale J, et al. F-18 labelled PSMA-1007: biodistribution, radiation dosimetry and histopathological validation of tumor lesions in prostate cancer. *Eur J Nucl Med Mol Imaging*, Published online October 26, 2016; <http://dx.doi.org/10.1007/s00259-016-3573-4>.