

Oncology

Complete biochemical response after stereotactic ablative radiotherapy of an isolated prostate cancer pelvic soft tissue recurrence detected by 18F-DCFPyL PET/CT



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1. Introduction

We report the management of a 67-year old gentleman with favorable intermediate risk prostate adenocarcinoma treated with definitive low dose rate brachytherapy who experienced biochemical recurrence nine years later. Although conventional imaging often fails to definitively identify sites of disease in this context, positron emission tomography/computed tomography (PET/CT) with small molecule radiotracers targeted against

prostate-specific membrane antigen (PSMA) have demonstrated significantly increased sensitivity for lesion detection in patients with recurrent/metastatic prostate cancer.^{1,2} This patient was found to have a solitary lesion on PSMA-targeted ¹⁸F-DCFPyL PET/CT and was treated with stereotactic ablative body radiotherapy (SABR) without initiation of androgen deprivation therapy (ADT). He experienced no significant complications and prostate-specific antigen (PSA) was undetectable at five month follow-up.

2. Case presentation

Our patient presented with a screening PSA of 5.3 ng/mL in 2007. Clinical exam demonstrated no palpable prostate disease or lymphadenopathy (clinical T1cN0) and prostate biopsy showed adenocarcinoma, Gleason 3 + 4 = 7 in 5% of 1 core (right apex) and 3 + 3 = 6 in 15% of 1 core (right lateral mid). He underwent low dose rate prostate brachytherapy for his favorable intermediate risk prostate cancer, receiving 122 ¹⁰³Pd seeds for a dose of 125 Gy. The patient's post-brachytherapy PSA nadir was 0.8 ng/mL.

In early 2016 his PSA rose to 3.5 ng/mL. Prostate biopsy was negative for malignancy. Magnetic resonance imaging (MRI) of the prostate in June 2016 showed a 3.6 × 2.1 × 2.7 cm prostate with brachytherapy seeds present but without suspicious morphology, enhancement, or restricted diffusion to suggest local recurrence and no suspicious lymphadenopathy. Whole body ^{99m}Tc-methylene diphosphonate bone scan demonstrated no uptake suspicious for osseous metastasis. His PSA continued to rise, reaching 4.4 in November 2016. Repeat MRI of the pelvis and bone scan in December 2016 again showed no evidence of recurrence or metastasis.

In January 2017 he underwent PSMA-targeted ¹⁸F-DCFPyL PET/CT which showed intense uptake (SUV_{max} 21.5) in a 2.6 × 2.3 × 1.1 cm soft tissue lesion along the inferior aspect of the right obturator internus musculature abutting the right ischioanal fossa which, in retrospect, could be identified on prior pelvic MRI (Fig. 1).

Abbreviations: PSMA, prostate-specific membrane antigen; ¹⁸F-DCFPyL, 2-(3-(1-carboxy-5-[(6-[¹⁸F]fluoro-pyridine-3-carbonyl)-amino]-pentyl)-ureido)-pentanedioic acid; PET, positron emission tomography; CT, computed tomography; SABR, stereotactic ablative radiotherapy; ADT, androgen deprivation therapy; PSA, prostate-specific antigen; ¹⁰³Pd, palladium-103, Gy, gray; MRI, magnetic resonance imaging; ^{99m}Tc, technetium 99m; SUV_{max}, maximum standardized uptake value.

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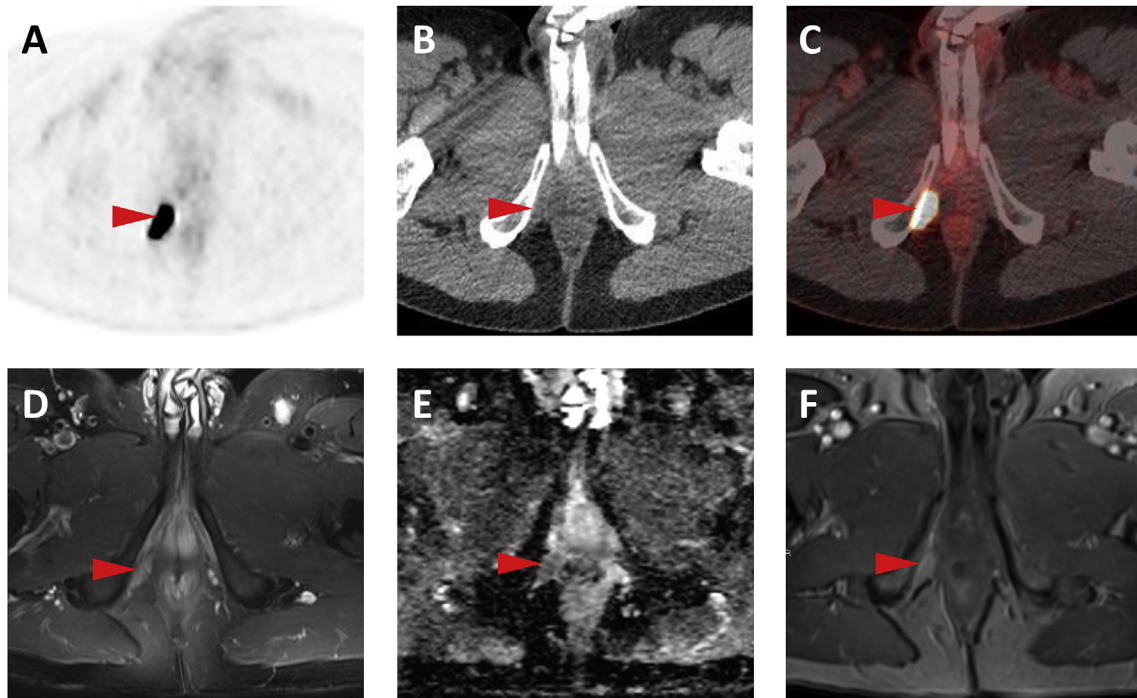


Fig. 1. (A) Axial PET, (B) axial CT, and (C) axial fused PET/CT images through the level of the ischiorectal fossae demonstrate intense radiotracer uptake fusing to subtle thickening adjacent to or within the right obturator internus musculature (red arrowheads). In retrospect, a corresponding abnormality can be seen on MRI including increased T2 signal, minimal restricted diffusion, and early contrast enhancement (red arrowheads on (D) axial fat-saturation T2-weighted image, (E) axial apparent diffusion coefficient image, and (F) axial dynamic contrast-enhanced T1 image). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

After initial consultation, his case was presented at the interdisciplinary tumor board at our institution. Group consensus was that his lesion would not be amenable to resection and that local consolidation with SABR with or without long-term ADT was reasonable. The site of presumed disease was deemed difficult to biopsy without significant risk of morbidity and tissue confirmation was not obtained. After discussion with the patient regarding his options, he opted to proceed with SABR in the absence of pathological confirmation of malignancy and to forego ADT.

He underwent CT-based radiation planning including anatomic correlation of the radiotracer-avid lesion to his planning CT. He received 36.25 Gy in 5 fractions prescribed to the 71.5% isodose line (Fig. 2). During treatment he reported grade I fatigue and lower urinary tract symptoms not requiring medical intervention. At 5-month follow-up, he denied any new urinary or bowel issues and had no evidence of disease with PSA <0.1 ng/mL and total serum testosterone of 226 ng/dL.

3. Discussion

This patient presented with biochemically recurrent prostate cancer without evidence of local recurrence or distant metastases initially identified on either MRI or bone scan. Due to the high sensitivity of PSA, biochemical failure often precedes the presence of detectable disease as assessed by conventional imaging modalities. While emerging modalities such as PSMA-targeted PET imaging afford higher sensitivity and thus earlier detection of recurrence,³ the clinical benefits of earlier intervention remain an active area of research.

While the standard of care for biochemical failure after brachytherapy without evidence of local failure is indefinite ADT, there is no agreed-upon PSA threshold for initiation of treatment despite an improvement in 5-year survival.⁴ Additional clinical factors arguing in favor of initiating ADT, such as rapid PSA doubling time, symptoms, or presence of detectable metastatic disease, must

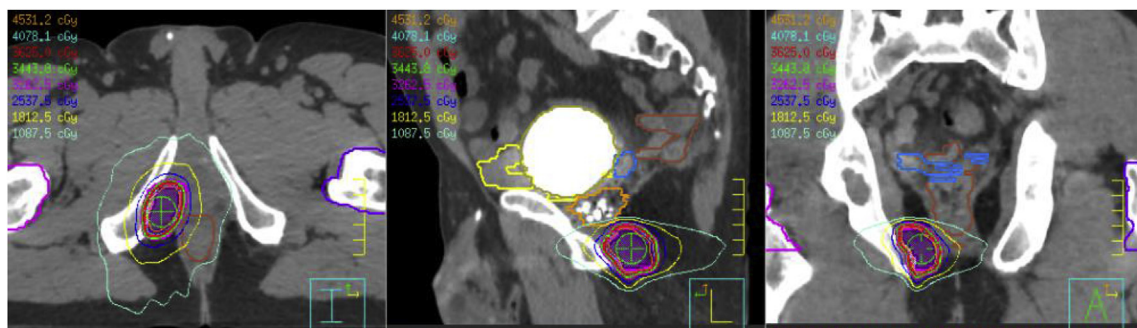


Fig. 2. Axial (left), sagittal (middle), and coronal (right) views of CT-based radiation plan for delivery of SABR to 3625 cGy in 5 fractions prescribed to the 71.5% isodose line. Radiolucent prostate brachytherapy seeds and penile prosthesis reservoir are visible on the sagittal view.

be weighed against the frequent, bothersome side effects of this systemic approach which include hot flashes, fatigue, decreased libido, erectile dysfunction, weight gain, elevated cardiac risk, and decreased muscle mass and bone density.

Early consolidation of all macroscopic tumor deposits with SABR is a promising approach to forestall ADT and perhaps provide a potentially curative intervention. SABR delivers highly targeted ablative-dose radiation to targets while minimizing exposure to surrounding organs at risk. Prior studies support metastasis-directed consolidation of low-volume metastatic prostate cancer with SABR as safe and highly effective, with local control rates exceeding 95%.⁵ While follow-up in this case is limited, our patient has to date had minimal toxicity and has achieved full biochemical response. Several randomized controlled trials are now investigating the clinical benefits of stereotactic ablative radiotherapy for patients with low-volume prostate cancer, including the Belgian STOMP (clinicaltrials.gov identifier NCT01558427), Baltimore ORIOLE (NCT02680587), British CORE (NCT02759783), Canadian PCS IX (NCT02685397), and French STEREO-OS (NCT03143322) trials. Continued developments in high-sensitivity, high-specificity imaging of prostate cancer will allow earlier target recognition and improve our likelihood of achieving total consolidation of disease before a low-volume process progresses to widely metastatic disease requiring systemic therapy. In this patient's case, the improved lesion detection ability of PSMA-based ¹⁸F-DCFPyL PET/CT allowed for the appropriate selection of a treatable lesion.

4. Conclusion

Herein we describe the use of PSMA-targeted ¹⁸F-DCFPyL PET/CT imaging to identify a solitary recurrence of prostate cancer not initially identified by MRI and subsequently treated with SABR. This patient achieved complete biochemical response with no significant treatment toxicity and without initiation of ADT. This case illustrates the value of targeted, high-precision diagnostic and therapeutic techniques as a compliment to standard approaches to management of biochemically recurrent prostate cancer.

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Informed consent

Written informed consent to publish this report was obtained from the patient described herein in accordance with Johns Hopkins Medical Institutions policy.

Conflicts of interest

MGP is a co-inventor on a US Patent covering ¹⁸F-DCFPyL, and as such is entitled to a portion of any licensing fees and royalties generated by this technology. This arrangement has been reviewed and approved by the Johns Hopkins University in accordance with its conflict-of-interest policies. MAG has served as a consultant to Progenics Pharmaceuticals, the licensee of ¹⁸F-DCFPyL. MAG, SPR, MGP, and KJP have received research support from Progenics Pharmaceuticals.

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