



Nuclear Medicine Pictorial Essay

Combined Intravenous Urogram and ⁶⁸Ga-PSMA PET/CT for Improved Staging and Restaging of Prostate Cancer

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ABSTRACT

Staging/restaging of prostate cancer utilizing Gallium-68 (⁶⁸Ga) prostate-specific membrane antigen (PSMA) positron emission tomography/computed tomography (PET/CT) in combination with an intravenous urogram allows improved discrimination between radiotracer activity in the renal tract and small pelvic nodes or local recurrences. Within this pictorial essay, we describe the imaging protocol utilized at our institution and present cases which demonstrate the utility of this combined imaging approach.

Keywords: Prostate cancer imaging, Prostate-specific membrane antigen positron emission tomography/computed tomography, Urogram, Prostate cancer staging, Positron emission tomography

INTRODUCTION

Staging and restaging of prostate cancer is critical in determining prognosis and strategies for disease management. Gallium-68 (⁶⁸Ga) prostate-specific membrane antigen (PSMA) positron emission tomography/computed tomography (PET/CT) has gained prominence for prostate cancer staging at Australian centers, as well as internationally. ⁶⁸Ga-PSMA PET/CT has shown high sensitivity and specificity for prostate cancer recurrence in several studies.^[1] However, at this time, no high-level evidence from randomized control trials is available. This situation, where adoption in clinical practice has outstripped the availability of high-level evidence, means each center offering ⁶⁸Ga-PSMA PET/CT will have a protocol based on their own experiences.

At our center, ⁶⁸Ga-PSMA PET/CT was introduced in June 2014. In April 2017, we updated our protocol to include a modified intravenous urogram. This method quickly became our standard practice, based on radiologist consensus that it enabled improved discrimination between radiotracer activity in the renal tract, normal variants, physiological uptake, and small pelvic nodes or local recurrences.

Imaging protocol

Our protocol commences with the administration of an intravenous (IV) bolus of 150–250 MBq ⁶⁸Ga-PSMA-11 ligand complex (1.8–2.2 MBq per kilogram of body weight) and an uptake period ranging from 45 to 60 min. Administration of 25 mL of IV contrast occurs 10 min before imaging

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acquisition. A low-dose CT (120 KeV and 10–30 mAs) is performed first, from the calvarial vertex to proximal thighs with the patient lying supine. Concurrent PET imaging is performed of the same region, commencing proximal thighs to calvarial vertex with 8–11 bed frames (depending on the length of the patient), with an acquisition time of 3 min/bed (4 min/bed over pelvis). Finally, a second dose of 75 mL of IV contrast is administered for the IVU and diagnostic CT, incorporating the pelvis, abdomen, chest, neck, and head. PET/CT systems are used for sequential low-dose CT, PET, and diagnostic CT image acquisition (Phillips Ingenuity TF 128 slice PET/CT, Phillips Healthcare, Amsterdam, Netherlands or GE Discovery MI DR PET/CT, GE Healthcare, Chicago, USA). Reconstructions on PET/CT emissions data are applied for attenuation correction, to minimize scatter and decay, reconstructions are also applied to diagnostic CT data. Further processing is done on appropriate workstations to create fusion images, MIPs, and plane reconstructions.

This protocol shows the contrast in the pelvic ureters and bladder 3 times over the imaging course, thus enabling a detailed assessment of high-risk structures, including both ureters with peristalsis, small nodes, and the bladder base. In early images, a small amount of contrast is seen in the pelvic calyceal systems and ureters. In mid images, contrast is seen in the pelvic arteries, the distal third of the ureters, and the bladder. In late images, contrast is seen in the aorta, inferior vena cava, pelvic arteries and veins, pelvic calyceal systems,

ureters, and bladder. Ultimately, this combined method allows for differentiation based on contrast opacification and PSMA uptake. For example, a malignant node adjacent to the ureter [Figure 1] or bladder [Figure 2] will show PSMA uptake and no contrast opacification, compared to the adjacent structures which will show both PSMA uptake and contrast opacification. Similarly, tumor recurrence at a surgical site, either from previous TURP [Figure 3] or prostatectomy [Figure 4], can be differentiated from surgical changes as the tumor will show PSMA uptake and no contrast opacification. Similarly, in Figure 5, PSMA uptake observed at a suspected site of tumor recurrence was difficult to differentiate from the adjacent non-dilated ureter. In this scenario, IVU imaging allows tracing of contrast opacification down the ureters, aiding in differentiation. Further, this imaging approach is of utility in assessing prospective radioligand therapy patients, as in addition to disease restaging, kidney function is also demonstrated [Figure 6].

DISCUSSION

Normal variants, physiological uptake, and excretion of ^{68}Ga -PSMA through the renal system present significant challenges in the assessment of ^{68}Ga -PSMA PET/CT examinations. This challenge is clinically important as pelvic lymph nodes and the bladder base are common sites of metastasis.^[2] Other authors have proposed alternative methods for this problem. These include the administration of furosemide concurrently

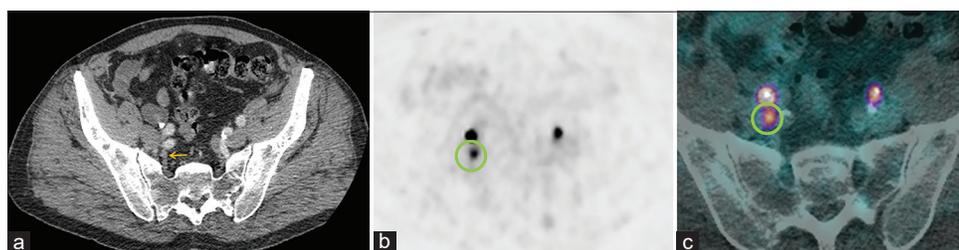


Figure 1: A 79-year-old male with newly diagnosed prostate cancer (Gleason 4+5, PSA 31 ug/L). (a) IVU imaging demonstrated contrast in both ureters. (b and c) PSMA PET demonstrated a small malignant right proximal internal iliac node measuring 5×3.2 mm showing intense PSMA uptake with maximum SUV of 26 and no contrast opacification (a, arrow). This node lies adjacent to the right ureter posteromedially, creating a “double dot” sign (b and c, circle).

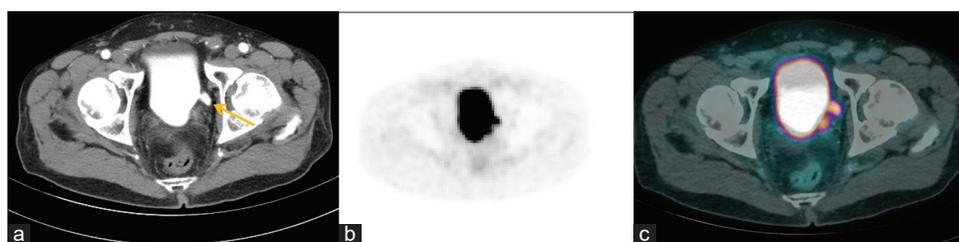


Figure 2: A 79-year-old male with prostate cancer in the setting of biochemical recurrence following radical prostatectomy and salvage radiotherapy (Gleason 4+5, PSA 0.4 ug/L). (a) IVU imaging demonstrated small elongated left posterolateral bladder diverticulum containing contrast (arrow). (b and c) PSMA PET imaging demonstrated small intensely avid tumor recurrence measuring 8×6.5 mm with a maximum SUV of 6.6. Tumor recurrence was adjacent to bladder and posteromedial to bladder diverticulum which also showed intense PSMA avidity.



Figure 3: A 77-year-old male with prostate cancer in the setting of biochemical recurrence following radical prostatectomy and pelvic node dissection (Gleason 4+3, PSA 1.2 ug/L). (a) IVU imaging demonstrated a small soft-tissue recurrence without contrast uptake measuring 10 × 8 mm in the surgical bed adjacent to the bladder (arrow). (b and c) PSMA PET imaging showed intense PSMA uptake of the recurrence with maximum SUV of 9.

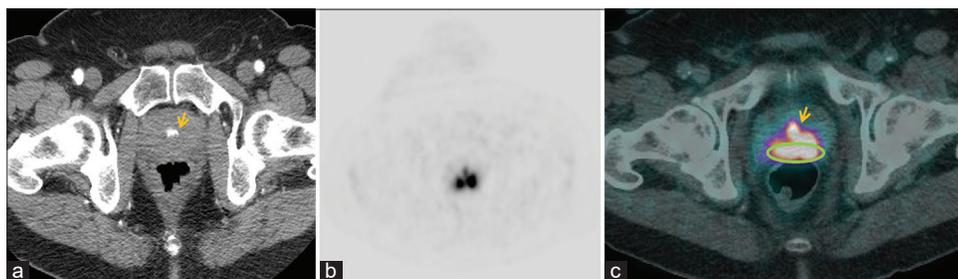


Figure 4: Staging in newly diagnosed prostate cancer (ISUP 5 + 5, PSA 27 ug/L). (a) IVU axial image shows prior TURP site demonstrating contrast uptake (arrow). (b and c) On PSMA PET primary tumor was located in PZ bilaterally in mid-prostate and demonstrated intense PSMA uptake with maximum SUV of 19 (c, circle). The TURP site also showed PSMA uptake (c, arrow).

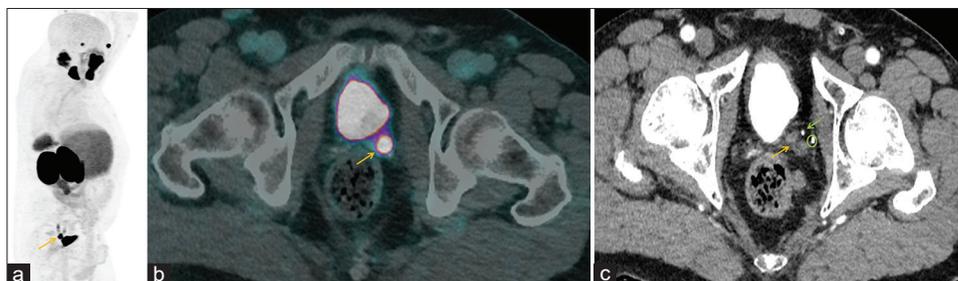


Figure 5: A 69-year-old male with prostate cancer in the setting of biochemical recurrence following radical prostatectomy (Gleason 4+5, PSA 0.51 ug/L). (a and b) PSMA PET images demonstrated an intensely avid region of soft tissue at prior resection site of the left seminal vesicle measuring 14 × 11.5 mm with a maximum SUV of 21 (orange arrows). This suspected recurrence was adjacent to the left ureter which was non-dilated. (c) IVU imaging allowed the non-dilated left ureter (green arrow) to be traced and thus differentiated from the tumor recurrence (orange arrow) and calcified phlebolith (green circle) also observed in the area.

with ⁶⁸Ga-PSMA;^[3,4] furosemide 60 min post-injection followed by delayed imaging at 180 min;^[5] and early pelvic images to avoid tracer accumulation.^[6] At our center, we do not utilize furosemide as this requires close attention to the patient's hydration status and can be limited by comorbidities that contraindicate the use of diuretics. Further, methods which incorporate large delays and multiple time-points are impractical in high-throughput centers, and those which incorporate early pelvic images can result in false negatives given low lesional uptake.^[6] Of note, a similar protocol to ours, combining ⁶⁸Ga-PSMA PET/CT and IVU, but without the diagnostic quality CT, have been reported by Iravani

et al., who retrospectively determined this approach assisted in the interpretation of 17.5% of cases.^[7] We believe that our imaging protocol is likely to improve the interpretation of a similar, if not higher, number of cases as our urogram protocol contains more phases, with the added advantage of also being able to detect other pathologies on the diagnostic CT component, as reported by McEwan *et al.*^[8] In this retrospective review of 1200 prostate cancer scans at our center, significant pathologies, often of greater clinical importance than the patient's prostate cancer, were identified in 5.7% of examinations due to the parallel interpretation of PET and diagnostic quality CT images.



Figure 6: A 74-year-old male with prostate cancer with a 5-year history of treatment failure presenting for assessment for Lutetium-177-PSMA radioligand therapy (PSA 53 ug/L). An undiagnosed left kidney obstruction was discovered. (a) IVU imaging showed delayed left nephrogram and pyelogram contrast opacification. (b and c) PSMA PET showed tracer build-up in obstructed kidney, secondary to a large left paraaortic lymph node impinging the mid-left ureter (arrow), extensive malignant retroperitoneal, and pelvic nodes also seen. A subsequent nuclear medicine renal scan with technetium-99m mercaptoacetyltriglycine ($^{99m}\text{Tc-MAG3}$) showed the left differential renal function of 22%.

CONCLUSION

There is no consensus regarding the optimal protocol for $^{68}\text{Ga-PSMA}$ PET/CT. Our method was implemented as an in-house solution to the difficulties posed by renal excretion of $^{68}\text{Ga-PSMA}$ and we do not have prospective data comparing our method with alternative imaging approaches. Within this pictorial essay, we present multiple examples of cases which would have presented significant interpretation difficulties if a combined protocol had not been utilized.

Declaration of patient consent

Patient's consent not required as the patient's identity is not disclosed or compromised.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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