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# Renal Cortical $^{68}$Ga-PSMA PET and $^{99m}$Tc-DMSA Images

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**Brief Title:** Renal cortical PSMA PET

**ABSTRACT**

$^{68}$Ga-prostate‑specific membrane antigen (PSMA) ligands are novel positron emission tomography (PET) radiotracers for prostate cancer. These radiotracers also localize in the normal renal cortex in a high degree and can demonstrate parenchymal defects. We recently started a prospective research to compare PSMA PET to $^{99m}$Tc-dimercaptosuccinic acid (DMSA) scan in adult patients with pyelonephritis. Here, we present a side by side comparison of renal cortical PSMA PET and DMSA images of a patient with chronic recurring pyelonephritis.

**Key Words:** DMSA scan, $^{68}$Ga-PSMA, PET, pyelonephritis, renal cortical

## INTRODUCTION

Technetium-99m-dimercaptosuccinic acid ($^{99m}$Tc-DMSA) scan is widely used to demonstrate renal parenchymal changes in pyelonephritis, particularly in detecting renal sequelae (scar formation) at least 4-6 months after acute infection (*1-3*). DMSA scan is more commonly used in pediatric population than adults. DMSA scan is the current gold standard in detecting renal scarring but it still has certain limitations such as relatively long waiting time after radiotracer injection, long acquisition time which is inconvenient for the patients, and limited spatial resolution of gamma cameras. In addition, there is a shortage of DMSA in certain countries, such as the United States, in the last few years (*4*).

Ga‑68 prostate‑specific membrane antigen ($^{68}$Ga-PSMA) ligands or inhibitors are novel positron emission tomography (PET) radiotracers to image prostate cancer and its metastases (*5-7*). The physiological biodistribution of $^{68}$Ga-PSMA ligands demonstrates uptake in various normal tissues, being highest in the kidneys and salivary glands (Fig.1). PSMA is a Type II transmembrane protein which is mainly found in prostate tissue and is overexpressed in prostate cancer as well as some other extraprostatic normal tissues including kidneys and various other malignancies (*8-10*). In immunohistochemical analysis, detectable PSMA levels were identified in a subset of proximal renal tubules (*8*). PSMA expression was available in the brush borders and apical cytoplasm of a subset of proximal tubules (*11*).

Assessing the kidneys in low-intensity settings on PSMA PET images shows a high degree uptake of the radiotracer in the renal parenchyma with high resolution images of the renal cortex (Fig.1) (*12-14*). In some of our patients with prostate cancer, PSMA PET also demonstrated renal parenchymal defects caused by various sizes of simple renal cysts which encouraged us to conduct a prospective study to compare PSMA PET to DMSA scan in adult patients with pyelonephritis

(*12-14*). Due to COVID-19 pandemic, our study is currently on hold but we wanted to present the PSMA PET and DMSA images of our first case.

**METHODS**

Our prospective study was approved by the Ethical Committee of Health Sciences Center at Kuwait University and Kuwait Ministry of Health. The study was conducted at Mubarak Al-Kabeer Hospital in Kuwait.

The patient provided written informed consent before the study. We obtained PSMA PET/CT and DMSA images from a 46 year-old female with history of chronic recurring pyelonephritis.

Radiolabeling of $^{68}$Ga-PSMA ligand (PSMA-11) was carried out at another institute (Radiopharmacy Unit at Kuwait Cancer Control Center) using 68Ge/68Ga generator and a manual synthesis module (Isotope Technologies Garching (ITG), Germany).

DMSA images were obtained 3 hours following intravenous injection of 111 MBq (3 mCi) $^{99m}$Tc-DMSA using Symbia S SPECT scanner (Siemens Healthineers, Erlangen, Germany) equipped with a high resolution parallel hole collimator. Multiple planar images in anterior, posterior, right posterior oblique and left posterior oblique projections (10 minute each, 20% window centered at 140 keV, 256 x 256 matrix and zoom 1.3) were obtained. Following planar imaging, SPECT images of the kidneys were obtained (20 second acquisition per view, 60 views, 360° rotation, 128x128 matrix, no zoom, 20% window centered at 140 keV). Images were reconstructed using a standard iterative algorithm and reformatted into transaxial, coronal**,** and sagittal views. Three days after DMSA scan, PSMA PET/CT images of the kidneys were obtained at Philips Time of Flight PET/CT camera (Philips Medical Systems, Best, Netherlands) 60 min following intravenous injection of 74 MBq (2 mCi) of $^{68}$Ga‑PSMA ligand. We used low activity to reduce radiation dose to patient and also due to limited amount of radiotracer. Before PET image acquisition, a low-

dose, unenhanced CT from region of the kidneys was obtained for attenuation correction, anatomic localization and gross anatomical correlation purposes. CT parameters included 30 mAs, 120 KV, 0.829 pitch, 0.5 sec rotation time, 64x0.625 collimation value and 5 mm slice thickness. PET acquisition time was 7 min/bed for 2 beds. Due to low dose activity administration image acquisition time was longer than usual. PET images were corrected for attenuation on the basis of the CT data and reconstructed using a standard iterative algorithm and reformatted into transaxial, coronal**,** and sagittal views. Maximum intensity projection images were also generated. Due to intense activity in the kidneys, PET images were reviewed in low intensity to better assess renal cortical uptake and distribution. Both attenuation corrected (AC) and uncorrected (non-AC) PET images as well as PET/CT fusion and low-dose CT images were evaluated to assess the anatomical location, size and morphology of the kidneys, uptake and distribution of radiotracer in the renal parenchyma, and to search for the parenchymal defects and other abnormalities.

**RESULTS**

The patient was a 46 year-old female with chronic recurring pyelonephritis in the last 10 years. In the last 2 month patient had an acute episode of pyelonephritis (positive urine culture for Escherichia coli) and treated with antibiotics for 2 weeks which was ended few days prior to this study.

DMSA images demonstrated slight cortical thinning with mildly reduced uptake in the upper pole of the right kidney without significant cortical defect (Fig. 2).

PSMA PET/CT images also demonstrated slight cortical thinning and mildly reduced uptake in the upper pole of the right kidney without a significant cortical defect (Fig. 3). Overall, there was excellent distribution of activity in renal cortices of the kidneys with more prominent uptake in the

renal columns on PSMA images. Image resolution was better with PSMA PET as compared to DMSA images.

Non-attenuation corrected (Non-AC) PSMA PET images also demonstrated the same findings with a reasonable image quality (Fig. 3).

Low dose CT images did not demonstrate simple cyst or calculi which can cause parenchymal defects.

**DISCUSSION**

Side by side comparison of renal PSMA PET and DMSA images in our first case demonstrate that $^{68}$Ga-PSMA ligand is promising as a renal cortical imaging radiotracer. PSMA PET has certain advantages over DMSA scan. Waiting period after radiotracer injection and image acquisition time is less with PSMA PET than those with DMSA scan. Images are obtained approximately 3 h after $^{99m}$Tc-DMSA injection and 1 h after $^{68}$Ga-PSMA ligand injection. Image acquisition time was approximately 14 minutes with PSMA PET/CT as compared to 45 minutes (20 min planar, 25 min SPECT) with DMSA scan in our case. In our case, PSMA PET image acquisition time was 7 min per bed due to a low dose radiotracer administration. Image acquisition time can be further reduced to 3-4 min with the administration of higher activity. Longer acquisition time with DMSA scan can cause patient discomfort and patient motion which result in image artifacts and may require obtaining additional images and sedation in pediatric patients. $^{68}$Ga has a shorter half-life (68 min) than $^{99m}$Tc (6 h). Absorbed adult kidney doses of $^{68}$Ga-PSMA-11 and $^{99m}$Tc-DMSA are 0.24 mGy/MBq and 0.18 mGy/MBq, respectively (*15,16*). Effective adult doses of $^{68}$Ga-PSMA-11 and $^{99m}$Tc-DMSA are 0.022 mSv/MBq and 0.0088 mSv/MBq, respectively (*15,16*). Injected activity of 111 MBq (3 mCi) of $^{99m}$Tc-DMSA and 74 MBq (2 mCi) of $^{68}$Ga-PSMA-11 yield an estimated

effective dose of 0.98 mSv and 1.63 mSv, respectively. This means that in adults $^{68}$Ga-PSMA-11 results in a 66% higher exposure of effective dose. There is an additional radiation dose from CT in PET/CT but CT is low dose and only covers kidney region. However, as the non-AC PET images also provide good quality images of the renal parenchyma, low-dose CT can be omitted. PET scanners offer higher spatial resolution than gamma cameras and can detect smaller defects (*17*). In our case, image resolution was better with PSMA PET (PET/CT and non-AC PET) than DMSA scan (planar and SPECT). SPECT/CT is expected to provide higher resolution images than SPECT, but we did not perform SPECT/CT in our case to reduce radiation dose to research patient. However, PET/CT is known to provide higher resolution images than SPECT/CT. On the other hand, new SPECT systems with cadmium zinc telluride (CZT) detectors have better resolution than conventional scanners with sodium iodide detectors.

The main limitations of PSMA PET imaging are higher cost, less global availability and higher radiation dose as compared to DMSA scan. However, amount of $^{68}$Ga-PSMA-11 activity may be further reduced with longer acquisition time (e.g. 37 MBq (1 mCi) and 10 min acquisition). The cost of DMSA scan and PSMA PET varies among institutes and countries. In our institute, the cost of DMSA scan and PSMA PET is approximately $292 and $454, respectively. However, currently there is a shortage of DMSA in certain countries. DMSA was added to the Drug Shortages List of the U.S. FDA in 2014 and was commercially unavailable thereafter (*4*). New renal cortical imaging radiotracers are needed as an alternative to DMSA scan or to replace it. In our early images, PSMA PET appears to have a potential to be an alternative to DMSA scan. $^{68}$Ga-Alizarin Red S was also studied in animals and humans as a renal cortical PET radiotracer in 1980s (*18*). PSMA PET provided comparable results to DMSA scan in our adult patient but we do not know its biodistribution and radiation dose in pediatric population. Further work is also required such as

understanding of the mechanism of uptake, the physiological meaning of uptake, determining the optimal injected activity, and dosimetry, before its use as renal cortical tracer can be supported.

## CONCLUSION

In our first case, PSMA PET provided promising results in an adult patient with pyelonephritis. Results of our prospective study in a higher number of adult patients will provide a more accurate comparison of PSMA PET to DMSA scan in pyelonephritis.

## DISCLOSURE

$^{68}$Ga-PSMA ligands are investigational PET radiotracers and as of now they have not been approved by the US Food and Drug Administration and European Medicines Agency. This is off-label use of $^{68}$Ga-PSMA ligands for renal imaging.

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**FIGURE LEGENDS**

**Figure 1:** $^{68}$Ga-PSMA-11 whole body maximum intensity projection (in high and low intensity settings) and selected coronal CT, PET and PET/CT fusion images (2 hr after iv injection of 129.5 MBq (3.5 mCi) $^{68}$Ga-PSMA-11) of a patient with prostate cancer demonstrates physiological high renal uptake and excellent distribution of activity in the renal cortex. Note an approximately 1 cm small cyst causing cortical defect in the upper pole of the right kidney (arrow).

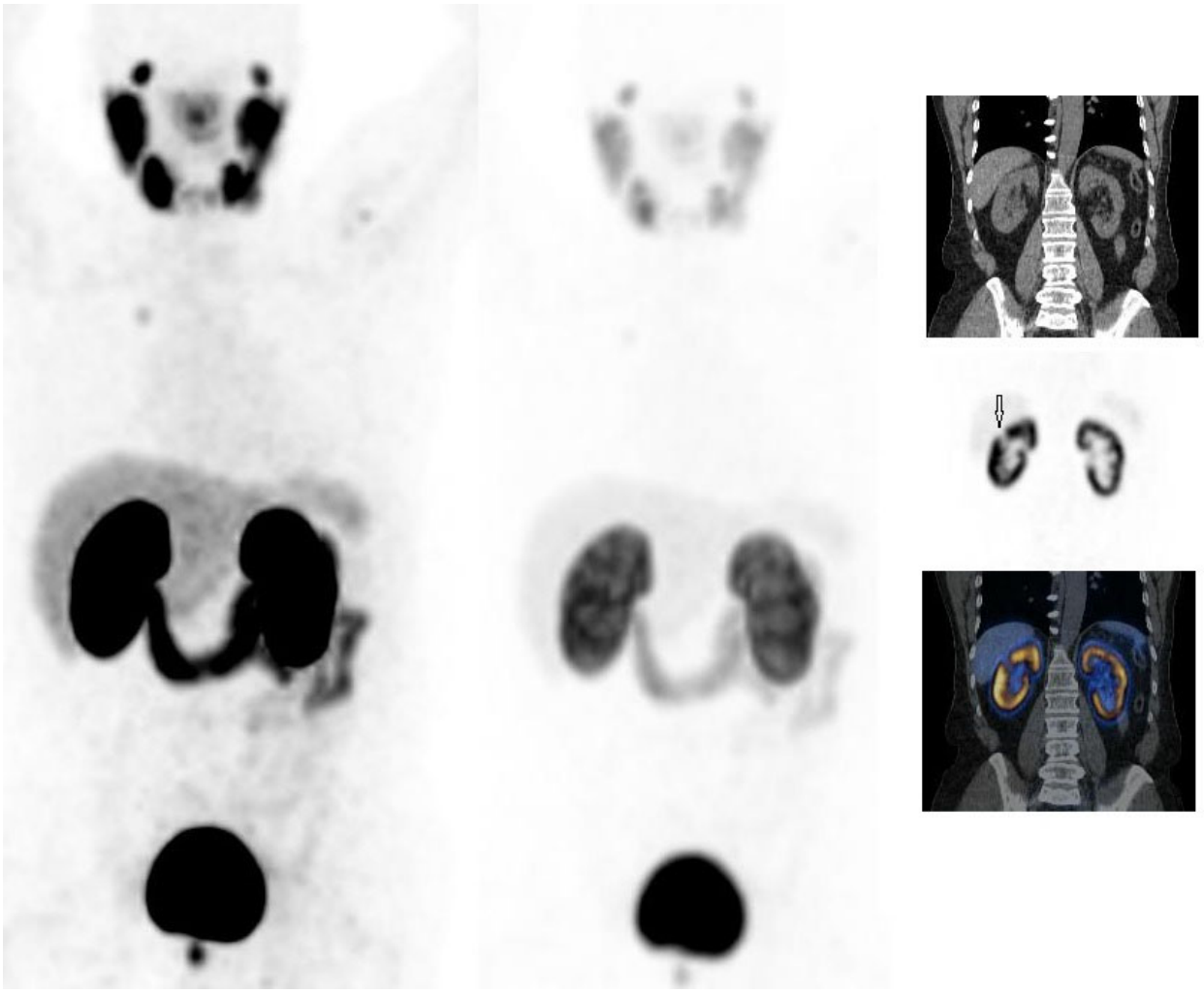

**Figure 2:** $^{99m}$Tc-DMSA planar (anterior, posterior, left posterior oblique, and right posterior oblique), and SPECT (selected coronal slices) images demonstrate slight cortical thinning and mildly reduced activity in the upper pole of the right kidney without a significant cortical defect.

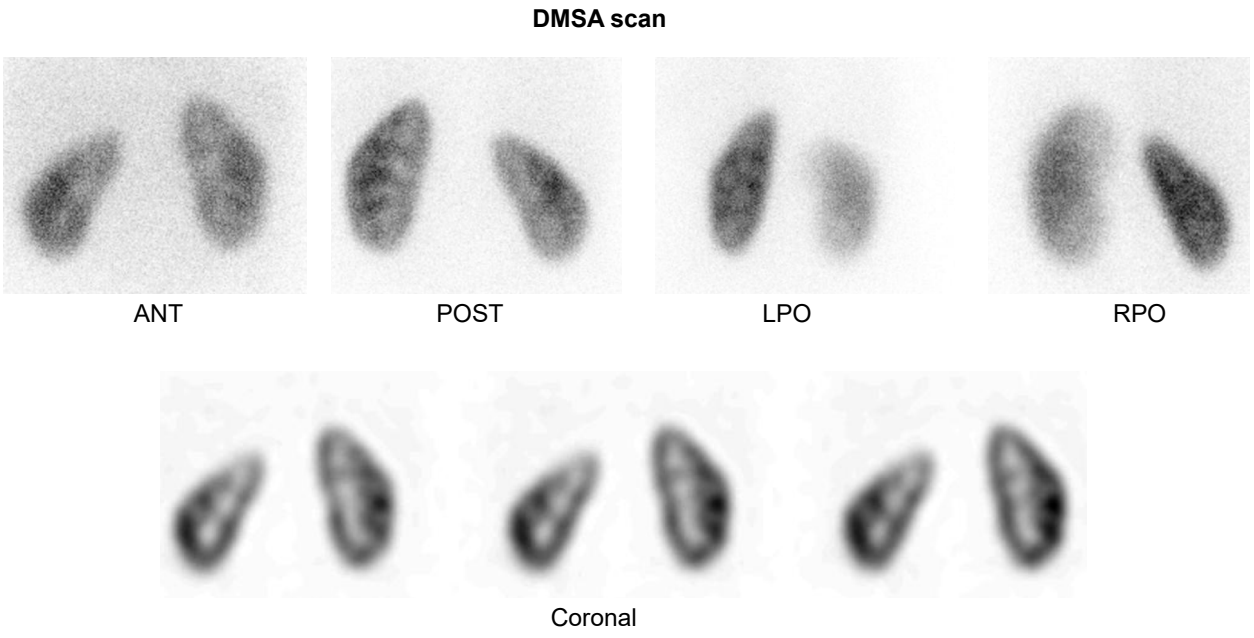

**Figure 3:** $^{68}$Ga-PSMA-11 maximum intensity projection, coronal PET/CT fusion, selected transaxial and coronal AC PET, and coronal non-AC PET images with an injected activity of 74 MBq (2 mCi). There is slight cortical thinning and mildly reduced uptake in the upper pole of the right kidney without a significant defect. Note the higher resolution images of the renal cortex with PSMA PET as compared to DMSA scan as seen in Fig. 2. Note that non-AC PET also provides good quality images of the kidneys.