Title

Pharmacokinetic Comparison of Selective Prostatic Arterial and Intravenous PSMA PET/CT Radioligand Infusions in Primary Prostatic Adenocarcinoma.

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Summary Statement

Selective prostatic arterial infusion yielded significantly higher radiotracer uptake in prostatic tumors than intravenous infusions when using dynamic prostate-specific membrane antigen PET/CT to simulate radioligand therapy.

Key Results

1. Prospective, intraindividual comparative study of five individuals with treatment-naïve prostate cancer who underwent two dynamic prostate-specific membrane antigen (PSMA) PET/CTs one week apart: a venous session followed by an arterial session.
2. Selective prostatic arterial infusion of ^{68}Ga-PSMA-11 achieved a 65.7-fold greater mean SUV_{max} (938.1 vs 14.3) in tumoral volumes-of-interest (VOIs) than intravenous infusions in the same patient (P = .008).
3. Areas under the SUV_{mean} curves were 60.9-fold greater (14599.7 vs 239.9 SUV*min) for arterial infusions (P = .002).

List of Abbreviations

AUC = area under the curve

IA = intra-arterial

IV = intravenous

PSMA = prostate-specific membrane antigen

SUV = standardized uptake value

TAC = time-activity curve

VOI = volume-of-interest

Abstract

Background: Intravenous PSMA-targeted radioligand therapy improves survival in men with metastatic castration-resistant prostate cancer. Yet, the impact of selective prostatic arterial administration on primary tumor uptake is unclear.

Purpose: To compare ^{68}Ga-PSMA-11 uptake using dynamic PET/CT in prostatic tumoral volumes-of-interest (VOIs) during intravenous and selective prostatic arterial infusions for individuals with untreated, high-risk prostate cancer.

Materials and Methods: In this prospective, intraindividual comparative study conducted at an academic medical center, five men aged 58, 61, 64, 66, and 68 years old with treatment-naïve prostate cancer were enrolled between January 2022 and February 2023 and underwent two dynamic ^{68}Ga-PSMA-11 PET/CTs one week apart. During the first scan, the radiotracer was administered intravenously. During the second scan, the radiotracer was delivered into the right or left prostatic artery through an angiographically-placed microcatheter. The primary outcome was maximum standardized uptake value (SUV_{max}) in prostatic tumoral VOIs. Secondary outcomes included mean SUV (SUV_{mean}) in prostatic tumoral VOIs and areas under the SUV_{mean} curves (AUCs). Longitudinal mixed effects models were used to compare dynamic SUV_{max} and SUV_{mean} curves, and paired t-tests were used for the remaining data.

Results: The mean SUV_{max} within tumoral VOIs was 14.3 (range, 2.9–42.8) for venous sessions and 938.1 (range, 459.6–1436.1) for arterial sessions (P = .008). SUV_{mean} within VOIs was greater during arterial sessions (P < .001) overall, and were

45.7-fold and 19.0-fold greater at peak uptake and final time points, respectively. Mean AUC was greater on arterial TACs than on venous TACs at 14599.7 SUV*min (range, 8353.0–20024.8) and 239.9 SUV*min (range, 68.6–621.8), respectively (P = .002).

Conclusion: Selective prostatic arterial infusion resulted in greater ^{68}Ga-PSMA-11 tumoral SUV than intravenous infusion in study participants. Further study of locoregional, intra-arterial delivery of a PSMA-targeted theranostic agent is warranted in high-risk prostate cancer.

ClinicalTrials.gov Identifier: NCT04976257

Introduction

Prostate-specific membrane antigen (PSMA)-based radioligand therapy (RLT) has emerged as an effective therapy in patients with metastatic castration-resistant prostate cancer (mCRPC) (1). While dose-limiting toxicities do exist, intravenously administered RLT with agents like ^{177}Lu-PSMA-617 is generally well-tolerated (2).

While the prostatic arteries offer a potential route for delivering locoregional therapy, selective arterial radioligand infusion for localized prostate cancer, to our knowledge, has not been evaluated. However, studies on gastroenteropancreatic neuroendocrine tumors have shown higher uptake in liver metastases with selective intra-arterial (IA) administration than intravenous (IV) when using ^{68}Ga-DOTATOC PET/CT to simulate therapy (3). If these findings translate to the prostate, selective prostatic IA infusion of a PSMA-based agent could lead to enhanced tumor uptake in patients with localized cancer.

Thus, this intraindividual comparative study aimed to compare 68Ga-PSMA-11 uptake using dynamic PET/CT in prostatic tumoral volumes-of-interest (VOIs) during IV and selective prostatic IA infusions for individuals with untreated, high-risk prostate cancer.

Materials and Methods

Study Design and Participants

All patients provided informed consent in this IRB-approved, single-arm, prospective, HIPAA-compliant pilot study (ClinicalTrials.gov Identifier: NCT04976257) conducted at the University of California, San Francisco Medical Center. The study used a within-person comparative approach and targeted participants with treatment-naïve prostate cancer via convenience sampling. The

inclusion and exclusion criteria are shown in Table 1. Five men aged 58, 61, 64, 66, and 68 years old with biopsy-proven prostatic adenocarcinoma and high or very high-risk histology were enrolled between January 2022 and February 2023 (Figure 1, Table 2).

Dynamic PET/CT and Angiographic Imaging Protocols

^{68}Ga-PSMA-11 was synthesized at our institution's radiopharmaceutical facility according to protocol using a precursor peptide mass of 5µg for each dose. The activity in each dose ranged from 7.0-7.7 mCi, and the injectate volumes ranged from 8-12 mL. All PET/CT imaging was performed on a Philips Vereos scanner (Philips Healthcare). All prostatic arterial catheterizations were performed in a Philips Azurion x-ray angiography suite (Philips Healthcare).

Venous Session

A localizer radiograph was obtained in the PET/CT scanner, and the 16.4 cm craniocaudal field-of-view was centered over the prostate. A ^{68}Ga-PSMA-11 dose was administered via infusion pump (Curlin 6000; Moog Medical) into an upper extremity peripheral IV at a continuous rate over 30 minutes. Dynamic PET images (144 x 144 matrix, 4mm x 4mm spacing) were acquired every minute during the 30-minute infusion and for 15 minutes after infusion (Figure 2). A whole-body diagnostic PET acquisition from vertex to mid-thigh was then obtained 60 minutes after the infusion start time, with emission data obtained from caudal to cranial at 2 minutes per bed position. A non-contrast CT scan was used for attenuation correction and anatomical reference from helically acquired raw images at kVp 120, pitch factor

0.7-0.8, 512 x 512 matrix, and 0.625mm single slice collimation using dynamic tube currents (Philips DoseWise).

Arterial Session

The arterial session was performed one week after the venous session. Prostatic arterial catheterization was performed by an interventional radiologist (R.K.) with 7 years of experience in prostatic artery embolization. Procedures were performed under local anesthesia with an external urinary catheter in place. Vascular access was obtained with ultrasound-guidance (Edge II, SonoSite), and a 5-French (Fr) vascular sheath (Brite Tip; Cordis) was placed into the common femoral artery ipsilateral to the side of the biopsy-proven prostatic tumor. For bilateral disease, the side with higher disease burden based on T2-weighted MRI was selected. A 5-Fr SIM-1 angiographic catheter (Cook Medical) was used to catheterize the ipsilateral internal iliac artery. Digital subtraction angiography using Omnipaque 350 (GE Healthcare) at 3ml per second was performed for 4 seconds in an ipsilateral 45-degree oblique projection. Cone-beam CT rotational arteriography was then performed at 2 ml per second for 10 seconds to characterize the arterial anatomy. The prostatic artery was selected with a 2.0-Fr straight-tip microcatheter (TruSelect; Boston Scientific) and shapable 0.014” guidewire (Synchro^2 Soft; Stryker). A hand-injected cone-beam CT was performed to confirm appropriate positioning in the main prostatic artery (supplying the entire hemiprostate) or a first order prostatic branch to the central gland or peripheral zone. The final microcatheter positioning was determined in real-time by the operator, with attention to suspected tumoral blood supply and microcatheter stability. Adhesive dressings were applied over the sheath and catheters to prevent movement.

Participants were transported by gurney to the PET/CT scanner. Stable positioning of the microcatheter was confirmed by a localizer radiograph. A ^{68}Ga-PSMA-11 dose was then administered through the microcatheter via infusion pump at a continuous rate over 30 minutes, and dynamic PET images were acquired using the same imaging parameters above. For Participant A, dynamic imaging was acquired for an additional 15 minutes post-infusion, and the microcatheter was cleared with 5mL of 0.9% sodium chloride over five minutes. For all subsequent participants, imaging was acquired for 30 minutes post-infusion without microcatheter flushing (Figure 2). A non-contrast helical CT scan was performed as above for attenuation correction and anatomical purposes.

Imaging Processing and Analysis

Image processing and analysis was performed (R.K.) on MIM Encore version 7.2.7 (MIM Software Inc). 2D regions-of-interest (ROIs) were manually drawn on consecutive slices from the non-contrast CT scan obtained during the venous session, reflecting the margins of the tumor on T2-weighted MRI or cine transrectal ultrasound. ROIs were limited to the side of arterial injection and did not cross the midline when bilateral disease was present. Software-based algorithms were employed to refine and smoothen the manual contours as needed. The series of 2D ROIs were subsequently combined to create a 3D tumoral VOI for each participant. This VOI was applied to both the venous and arterial CT datasets.

The venous and arterial dynamic PET datasets were manually inspected for motion. Manual re-alignment using translation, rotation, or both, was employed as necessary. Attenuation- and motion-corrected dynamic PET volumes were then

superimposed on their corresponding anatomical CT volumes, and the raw 1-minute PET data within the tumoral VOIs were averaged into 3-minute frames.

Statistical Analysis

The primary outcome measure was SUV_{max} within prostatic tumoral VOIs for each TAC. Secondary outcome measures included SUV_{mean} TACs, on which peak values ($SUV_{mean\text{-}peak}$) and final time points ($SUV_{mean\text{-}washout}$) were determined. Other secondary outcome measures were time to SUV_{max} (T_{SUVmax}) and areas under the SUV_{mean} curves (AUCs) within tumoral VOIs. Statistical analyses were performed in R (Version 4.3.1; R Core Team) by two authors (X.W. and R.K.). The venous and arterial SUV_{max} and SUV_{mean} curves were compared using longitudinal mixed effects models. T_{SUVmax} and AUC data were compared using paired sample t-tests. A two-sided P value of less than 0.05 was considered statistically significant. A paired sample t-test power analysis estimated that a mean SUV_{max} difference of 1.68 times the standard deviation would be detected with 80% power, assuming a two-sided alpha of 0.05.

Results

All participants completed the imaging protocol without adverse events. For every IA session, the arterial microcatheter was positioned distal to extraprostatic collaterals. Hypermetabolic pelvic or iliac lymph nodes above background were incidentally identified in two participants (A and E), and these results are discussed in Appendix S1.

Time-Activity Curves

The SUV_{max} and SUV_{mean} TACs are shown in Figure 3 and Figure 4, respectively. For venous sessions, the TACs were approximately linear, with gradual accumulation of ^{68}Ga-PSMA-11 in the VOI. TACs from arterial sessions were characterized by rapid early upstrokes followed by plateauing during the infusion with subsequent washout. For Participant A, both the IV and arterial microcatheter were flushed with saline shortly after the 30-minute infusions. This accounts for the second peak in arterial SUV_{max} and SUV_{mean} during the post-infusion period (Figure S1), which subsequently returned to baseline over several minutes. For outcomes analysis, these datapoints were excluded, and interpolated data was generated based on dynamic datapoints before and after the event. These changes are reflected in Figure 3 and Figure 4. Flushing was not performed after either dose administration for other participants, and no correction was necessary.

Outcome Measures

The results for all outcome measures are shown in Table 3. The mean SUV_{max} within tumoral VOIs was 14.3 (range, 2.9–42.8) for venous sessions and 938.1 (range, 459.6–1436.1) for arterial sessions, corresponding to a mean 65.7-fold increase ($P = .008$). Peak accumulation in tumoral VOIs was noted sooner during arterial sessions, with a mean T_{SUVmax} of 15.0 min (range, 11–20), versus a mean T_{SUVmax} of 48.4 min (range, 41–60) for venous sessions ($P < .001$). AUC was 60.9-fold higher for arterial sessions than venous sessions, with mean values of 14599.7 SUV*min (range, 8353.0–20024.8) and 239.9 SUV*min (range, 68.6–621.8), respectively ($P = .002$). SUV_{mean} values were significantly greater over the imaged time points ($P < .001$), while $SUV_{mean\text{-}peak}$ and $SUV_{mean\text{-}washout}$ were 45.7-fold and 19.0-fold greater, respectively. Representative imaging is shown in Figure 5 and Figure 6.

Discussion

This proof-of-concept study used an intraindividual design to compare IV and selective prostatic IA radioligand uptake in five participants with high-risk, untreated prostatic adenocarcinoma. We demonstrated that the mean SUV_{max} was nearly 66-fold higher with selective prostatic IA administration than IV infusions (938.1 vs 14.3; P = .008) when using ^{68}Ga-PSMA-11. Areas under the SUV_{mean} curves were 60.9-fold greater (14599.7 vs 239.9 SUV*min; P = .002) for arterial infusions, suggesting a higher number of receptor binding events during the dynamic PET/CT scan. Saturation kinetics in the tumor were observed during each IA infusion.

Neoadjuvant IV ^{177}Lu-PSMA-617 for localized prostate cancer is currently being explored (4). Our findings highlight the need to investigate other routes of delivery that could enhance uptake in primary prostatic tumors , as studies have shown correlations between pre-treatment ^{68}Ga-PSMA-11 SUV and tumoral absorbed dose with radioligand therapy (5, 6). Locoregional IA RLT using a PSMA-based agent would be feasible in most patients, since bilateral prostatic artery catheterization is routinely achievable during prostatic artery embolization. In keeping with previous studies, the tumor TACs for IV administrations rose gradually (7) and did not intercept the IA TACs, suggesting a persistent subsaturated state at the imaged IV time points (8). Though the final PET/CT data was acquired at 1 hour, additional tumoral uptake at 3 hours would likely be small (9-11), and beyond 3 hours may begin to decline (12). Additional studies with a true theranostic agent will be needed to evaluate the amplified tumoral uptake we have demonstrated with IA infusions over IV infusions, however.

Locoregional delivery of theranostic agents requires special dosimetry considerations, as administration of peptide masses exceeding the target tissue binding capacity will result in systemic circulation of the radioligand. To replicate the IA pharmacokinetics observed herein for locoregional prostate cancer therapy, it may be necessary to administer no more than a 5μg ligand mass on each side, comparable to current ^{68}Ga-PSMA-11 doses. PSMA-617 ligand masses for theranostic preparations at our institution are typically 150μg (i.e. 30-fold greater); thus, a proportional reduction of PSMA-617 amounts may be required for the IA route. Targeted alpha therapy (TAT) may be particularly suited for the IA route, given that a single nuclear traversal with an α-particle can lead to cell death (13) and the small activities injected would require much lower ligand masses for delivery. While TAT radioligands such as ^{225}Ac-PSMA-617 have shown to be efficacious in mCRPC (14, 15), their ability to treat localized disease, regardless of administration route, has not been studied to our knowledge.

Our proof-of-concept study has several limitations. First, the results may only be applicable to IA infusions with small PSMA peptide masses, and therapeutic efficacy cannot be estimated using ^{68}Ga-PSMA-11 alone. Second, whether IA dosimetry would limit uptake in distant metastatic lesions remains unknown, as we were unable to quantify the radioligand uptake outside of the pelvis during arterial sessions. Third, delayed imaging was not performed in this study, which could underestimate the venous SUV endpoints. Finally, the administration of high activity into a small perfused volume, coupled with the limited spatial resolution of ^{68}Ga PET imaging, did not allow for accurate SUV quantification in the non-tumoral prostate or directly adjacent structures such as the bladder or rectum due to blurring.

In conclusion, using dynamic PET/CT, selective prostatic arterial infusion of ^{68}Ga-PSMA-11 resulted in greater tumor SUVs than intravenous infusion in study participants with high-risk prostate cancer. This warrants additional research into locoregional PSMA radioligand delivery.

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Tables

Table 1: Inclusion and Exclusion Criteria

Inclusion Criteria
Age greater than or equal to 18 years and less than or equal to 80 years
Ability to provide informed consent
Biopsy-proven unilateral or bilateral prostate adenocarcinoma, any stage (any N, any M)
Maximal tumor diameter ≥ 1.5cm on one or two affected sides, documented on prostate MRI or TRUS within 4 months of first scan
High or very high-risk histologic grade group by NCCN criteria on biopsy performed within 4 months of first scan
Exclusion Criteria
BMI > 35
Prior treatment for prostate cancer, or any use of anti-androgen therapy within 3 months of first scan
History of any pelvic radiotherapy
Severe atherosclerosis from prior CT imaging study, or greater than 10 pack-year smoking history if no prior imaging available
Stage IV or V chronic kidney disease by eGFR within 45 days of first scan
Platelet count < 50 x 10^9/L and/or International Normalized Ratio > 1.5
Severe allergy to iodinated contrast
Active urinary tract infection or recent episode of prostatitis within 1 month of first scan
Inability to tolerate prolonged supine positioning

BMI: body mass index, calculated as weight in kilograms divided by height in meters squared; eGFR: estimated glomerular filtration rate; NCCN: National Comprehensive Cancer Network; TRUS: transrectal ultrasound

Table 2: Characteristics of Five Study Participants

Characteristic	Participant A	Participant B	Participant C	Participant D	Participant E
Demographic Characteristics					
Age (y)	64	66	68	61	58
BMI	24.1	27.1	26.9	24.3	26.5
Imaging Characteristics					
Modality	MRI	MRI	MRI	MRI	TRUS
Side of tumor	Right > Left	Right > Left	Right	Right	Left
Location of tumor involvement	Posteromedial midgland and lateral apical PZ (right); posteromedial midgland (left)	Anterior midgland and apical PZ, TZ, and stroma (right); apical PZ, TZ, and stroma (left)	Posterior base, midgland, and apical PZ	Posterior base and midgland PZ	Posterolateral base and midgland PZ
Maximum dimensions (ML x AP x CC) (cm)	2.2 x 1.5 x 2.9	2.0 x 1.8 x 1.8	1.7 x 1.5 x 3.1	1.8 x 1.0 x 1.5	1.5 x 1.0 x 0.9
Pathologic Characteristics					
Serum PSA (ng/mL)	7.3	10.8	2.3	41.6	4.7
Biopsy Gleason score	9 (4+5)	9 (4+5)	8 (4+4)	9 (5+4)	8 (4+4)
Final staging	T3bN1M0	T3aN0M0	T3aN0M0	T3aN0M0	T3bN1M0
Final Gleason score	9 (4+5)	9 (4+5)	9 (4+5)	N/A (radiation only)	7 (4+3)

IA Procedural Characteristics					
Fluoroscopy time (min)	12.2	18.2	10.0	9.4	11.2
Side of catheterization	Right	Right	Right	Right	Left
Location of infusion in prostatic artery	Posterior branch	Anterior branch	Common trunk	Posterior branch	Posterior branch

Gleason score is determined by grading the two commonest histologic patterns in a prostate cancer specimen (using a 1 [low grade] - 5 [high grade] scale) and adding the two grades together. As only a portion of the tumor may be sampled during biopsy, the final Gleason score may be upgraded or downgraded after assessment of the full prostatectomy specimen. ‘Final staging’ T and N were determined surgically, and M was based on the whole-body prostate-specific membrane antigen (PSMA) PET/CT results. For Participant D, who opted for radiation therapy, T-staging was determined by prostate MRI and TRUS, and N and M-staging by PSMA PET/CT. ‘Tumor dimensions’ refers only to the tumor dimensions ipsilateral to the side of arterial catheterization. ‘Location of infusion in prostatic artery’ indicates whether the anterior or posterior branch was selected, or if the infusion was administered into the common trunk giving rise to both the anterior and posterior branches. AP: anteroposterior; BMI: body mass index, calculated as weight in kilograms divided by height in meters squared; CC: craniocaudal; IA: Intra-arterial; ML: mediolateral; PSA: prostate-specific antigen; PZ: peripheral zone; TRUS: transrectal ultrasound; TZ: transition zone

Table 3: Summative Time-Activity Curve Data in Tumoral VOIs from Intravenous and Selective Prostatic Arterial ^{68}Ga-PSMA-11 Infusions

Outcome	Venous	Arterial	P value
SUV_{max}	14.3 (+/- 16.2)	938.1 (+/- 371.5)	P = .008
$SUV_{mean\text{-}peak}$	9.7 (+/- 5.0)	443.4 (+/- 188.6)	P < .001
$SUV_{mean\text{-}washout}$	9.4 (+/- 5.0)	179.0 (+/- 112.9)	P < .001
T_{SUVmax} (min)	48.4 (+/- 10.6)	15.0 (+/- 3.5)	P < .001
AUC (SUV * min)	239.9 (+/- 218.0)	14599.7 (+/- 4164.1)	P = .002

Standard deviation is reported in parentheses. P values comparing venous and arterial datasets for SUV_{max} and SUV_{mean} endpoints were calculated using longitudinal mixed effects models. P values comparing venous and arterial datasets for T_{SUVmax} and AUC endpoints were calculated using paired sample t-tests. SUV_{max}: maximum standardized uptake value on time-activity curve; $SUV_{mean\text{-}peak}$: mean SUV within VOI at time of greatest uptake; $SUV_{mean\text{-}washout}$: mean SUV within VOI at final imaged time point; T_{SUVmax}: time to maximum SUV on time-activity curve; AUC: area under the SUV_{mean} curve; VOI: volume-of-interest

Supplemental Table 1: Comparison of SUV_{mean} ^{68}Ga-PSMA-11 Time-Activity Curve Data in Tumoral VOIs at Peak and Final Time Points, by Participant

	Participant A	Participant B	Participant C	Participant D	Participant E
VOI Characteristic					
Size (cm^3)	6.3	4.9	4.7	3.2	1.7
Voxel counts*	Venous N= 100 Arterial N = 98	Venous N = 75 Arterial N =76	Venous N = 74 Arterial N = 74	Venous N = 51 Arterial N = 50	Venous N = 25 Arterial N = 26
$SUV_{mean-peak}$					
Venous	21.6 (+/- 8.8)	5.0 (+/- 1.4)	4.5 (+/- 1.0)	4.7 (+/- 2.0)	2.0 (+/- 0.4)
Venous mean-peak time (min)	60	38	43	60	39
Arterial	455.4 (+/- 246.8)	470.7 (+/- 157.1)	287.5 (+/- 72.5)	427.4 (+/- 195.7)	793.2 (+/- 229.8)
Arterial mean-peak time (min)	21	14	19	21	13
$SUV_{mean-washout}$					
Venous	21.6 (+/- 8.8)	4.0 (+/- 1.4)	4.2 (+/- 0.9)	4.7 (+/- 2.0)	1.9 (+/- 0.2)
Arterial	431.1 (+/- 199.5)	58.2 (+/- 22.8)	56.0 (+/- 10.3)	118.0 (+/- 59.8)	49.6 (+/- 15.0)

Standard deviation reported in parentheses. *VOIs were placed on an anatomical basis, independent of the PET matrix. Thus, the number of PET voxels included within the VOI was allowed to vary slightly between arterial and venous sessions. SUV: standardized uptake value; VOI: volume-of-interest; CC: craniocaudal

Figure Legends

Figure 1: Flowchart shows the number of men with prostate cancer assessed for eligibility along with those deemed ineligible or who declined to participate. TRUS: transrectal ultrasound.

Figure 2: Imaging protocol diagram. Whole-body PET/CT images obtained during venous sessions were timed to acquire the prostatic bed position 60 minutes after ^{68}Ga-PSMA-11 infusion initiation.

Figure 3: SUV_{max} time-activity curves for prostatic tumoral VOIs, by participant and phase. Inset graph shows the terminal datapoints for venous sessions on a smaller scale, including the final VOI values obtained during whole-body PET scans at 60 minutes. For Participant A, dynamic PET imaging was performed for 45 minutes during the arterial session. For subsequent participants, 60 minutes of dynamic PET imaging was performed during arterial sessions. VOI: volume-of-interest.

Figure 4: SUV_{mean} time-activity curves within prostatic tumoral VOIs, by participant and phase. Inset graph shows the terminal datapoints for venous sessions on a smaller scale, including the final VOI values obtained during whole-body PET scans at 60 minutes. For Participant A, dynamic PET imaging was performed for 45 minutes during the arterial session. For subsequent participants, 60 minutes of dynamic PET imaging was performed during arterial sessions. VOI: volume-of-interest.

Figure 5: Cross-sectional and angiographic imaging in a 66 year-old male (Participant B) with Gleason 4+5 prostate cancer centered in the anterior apices and fibromuscular stroma, right greater than left. A, Axial T2 MRI and B, dynamic contrast-enhanced axial T1 MRI images demonstrate the prostatic tumor. The right-sided portion of the lesion is outlined in pink. The left-sided portion of the tumor (star) was excluded from the manually drawn VOI per protocol. C, Digital subtraction angiography of

the anterior branch of the right prostatic artery (solid arrow) with tumoral hyperenhancement (triangle). There is reflux into a prostatorectal trunk (dashed arrow) supplying the peripheral zone. D, Axial cone-beam CT angiogram image confirms arterial enhancement in the expected location of the tumor (pink outline). The anterior (solid arrow) and posterior (dashed arrow) branches of the prostatic artery are also visualized.

Figure 6: Dynamic PET/CT and pathologic images for the same participant as in Figure 5. A, Axial dynamic PET/CT image acquired during intravenous administration of ^{68}Ga-PSMA-11 demonstrates the hypermetabolic primary prostatic tumor. The right-sided portion of lesion used for VOI analysis is outlined in pink, reflecting the margins seen on prior T2 MRI. Tumoral radiotracer uptake extends across midline into the left anterior apex (star). B, Axial dynamic PET/CT image acquired during selective right prostatic arterial administration of ^{68}Ga-PSMA-11 demonstrates intense radiotracer uptake in the VOI outlined in pink. There is comparatively minimal uptake in the unperfused left-sided portion of the tumor (star). The arterial sheath and catheters in the right groin are partially visualized (arrow). C, Hematoxylin and eosin staining of the prostatic apex after radical prostatectomy, unmagnified. The midline (dotted line) and dominant tumoral margins (solid line) are shown. Small additional areas of carcinoma (squares) without T2 MRI correlates were also identified pathologically.

Supplemental Figure 1: Original and corrected SUV_{max} (A) and SUV_{mean} (B) time-activity curves for Participant A, a 64 year-old male with Gleason 4+5 prostate cancer involving the posteromedial midgland peripheral zones bilaterally and the right lateral apical peripheral zone. Raw acquisition data demonstrated a rise in arterial SUV_{max} and SUV_{mean} from minutes 31 to 33 due to post-infusion microcatheter flushing. As a correction, the raw values at minute 31 were applied to those at minute 32. Each subsequent raw data point (from minutes 33 – 45) was decreased by the absolute rise in SUV_{max} or SUV_{mean} from minute 31 to 33. Voxels from the raw 1-minute frames were averaged into 3-minute frames after the corrections. Given the magnitude of the

difference between arterial and venous endpoints across all participants, it is unlikely that alternative methods of data correction would change the outcome of the study.