

Can SUV_{max} of ^{68}Ga -labeled PSMA Ligand and ^{18}F -choline PET/CT Be Used to Predict the Radiation Dose in Prostate Cancer Patients?

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Abstract—Gallium-68 (^{68}Ga)-PSMA and ^{18}F -Choline are two radionuclides that have already shown high potential for the detection of prostate cancer. The comparison between these two radionuclides has several advantages in radiation protection. The aim of this prospective study was to identify which of these two radionuclides can help in predicting the equivalent dose using the maximum standard uptake value (SUV_{max}) of normal organs, the kidneys. Two groups of 40 patients (total $n = 80$) who underwent PET/CT using ^{68}Ga or ^{18}F for diagnosis of prostate cancer between April 2018 and December 2018 at the American University of Beirut Medical Center were included. First, the dose rates were measured after 1 h of radionuclide uptake at 1 m distance with background of $0.015 \mu\text{Sv h}^{-1}$. Then, SUV_{max} for kidneys were determined from images obtained with PET/CT 1 h after injection of both radionuclides. The ratios of the equivalent doses to the SUV_{max} for kidneys were compared for both ^{68}Ga -PSMA and ^{18}F -Choline. There is a positive moderate relationship between the SUV_{max} for kidneys and the ^{68}Ga dose rate after 1 h of injection at 1 m distance from the abdomen (p -value = $0.023 < 0.05$). This relationship is statistically significant. However, there is a very low negative relationship between the SUV_{max} kidney and ^{18}F dose rate after 1 h of injection at 1 m distance from the abdomen (p -value = $0.93 > 0.05$). This relationship is not statistically significant. This leads to the suggestion that we can predict the equivalent dose due to ^{68}Ga by indicating the SUV_{max} from the PET/CT images. *Health Phys.* 120(1):80–85; 2021

Key words: cancer; dose; dose equivalent, effective; radiation protection

INTRODUCTION

RADIATION USED for medical purposes has value for patients in diagnosing and treating disease. Since the amount of radiotracer used in nuclear medicine tests is extremely small,

the patient's radiation exposure is minimal. In nuclear medicine, the ALARA principle (As Low As Reasonably Achievable) is used to determine the amount of radionuclide with the least amount of radiation exposure to the patient. Radiation dose is a measure of the amount of exposure to radiation (Benedetto 1987) where the equivalent dose is used in radiological protection to specify the exposure limits and compare its value with the health effects. Prostate cancer (PC) represents the most common cancer in men and accounts for the third most common cause for cancer-associated death in men (Torre et al. 2015). Imaging plays an important role in the imaging evaluation of every phase of prostate cancer. One of the most commonly used nuclear medicine exams is Positron Emission Tomography/Computed Tomography (PET/CT), which has been one of the critical steps forward in practicing individualized medicine in prostate cancer management (Obek et al. 2017). Its undoubted advantages are valuable in clinical oncology as well as in all fields of diagnosis, staging, and treatment (Saif et al. 2010). The use of radionuclides in PET/CT scanning requires the application of radiation safety measurements and the commitments of the maximum limit of the radiation for the patient and hospital staff as recommended by the International Commission on Radiation Protection (ICRP) organization (Demir et al. 2010). Several radionuclides have been proposed for molecular imaging of PC including ^{18}F -Choline and ^{68}Ga -PSMA. Gallium-68 is most often obtained from a $^{68}\text{Ge}/^{68}\text{Ga}$ generator system. Gallium-68 decays with 89% yield by positron emission and has a half-life of 67.71 min (ICRP 2008). Fluorine-18-Choline is becoming more widely available with a longer half-life of 109.771 min (ICRP 2008) and the emission of high energy positrons when decaying (Grant et al. 2008). The standardized uptake value (SUV) is a dimensionless ratio used by nuclear medicine professionals to distinguish between “normal” and “abnormal” levels of uptake. It is defined as the ratio of activity per unit volume of a region of interest (ROI) to the activity per unit whole body volume and is considered a semi-quantitative parameter. For diagnosis, SUV

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The authors declare no conflicts of interest.

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has been useful for determining whether an area of uptake should be reported as suspicious for malignancy (Mah and Caldwell 2008).

The objective of this study was comparing two different radionuclides, ^{68}Ga -Prostate-Specific Membrane Antigen (PSMA) and ^{18}F -Choline used for detection of prostate cancer, to determine if the kidneys' maximum standardized uptake value (SUV_{max}) value can be used as an indicator of the equivalent dose to the patient.

MATERIALS and METHODS

This was a prospective study where we originally selected 40 male patients who underwent ^{18}F -Choline-based PET/CT and 40 male patients who underwent ^{68}Ga -PSMA PET/CT between April 2018 and December 2018.

Dose rate measurements and image analysis

On the day of the exam, and after the preparation of radiotracers, each patient is injected with a bolus containing either a dose between 84.36 MBq and 131.72 MBq (mean dose = 111 MBq) of ^{68}Ga -PSMA or a dose between 259.00 MBq and 329.30 MBq (mean dose = 298.22 MBq) of ^{18}F -Choline. The patient rests for 40 min after the injection. Before undergoing the PET/CT imaging, the patient is asked to empty the bladder. The patient is imaged for 20 min from the base of the skull to the mid-thighs using the PET/CT scanner. Data were acquired for 2.5 min per bed position with 120 kV and 180 mAs for the CT scan. PET data were reconstructed using VUEPointHD ViP (VPHD) algorithm with image matrix size of 192×192 (4-mm pixel spacing).

A Ludlum-Model 2241-3 (Ludlum Measurements, Sweetwater, TX) survey meter with GM detector was used for the measurements of the dose rates. The dose rate at 1 m distance from the abdomen of each patient was measured after 1 h of ^{68}Ga -PSMA and ^{18}F -Choline injections to the patients with a background of $0.015 \mu\text{Sv h}^{-1}$. PET images

were reviewed, and SUV_{max} for kidneys were determined from images obtained with PET/CT 1 h after injection of both ^{68}Ga -PSMA and ^{18}F -Choline radionuclides.

Data acquisition

SUV_{max} for kidneys and patient's dose rates at 1 m distance from the abdomen of each patient and after 1 h measurements were noted. SUV_{max} for kidneys were correlated with dose rates of each radionuclide in a patient-based analysis. The obtained results of ^{68}Ga -PSMA and ^{18}F -Choline were compared.

Statistical analysis and mathematical calculation

Descriptive statistical analysis was performed with the statistical program SPSS, version 25.

Study variables were stratified as numerical. Numerical variables were calculated as means and standard deviations and also presented as minimum and maximum values as shown in Table 1. The p value is the probability of obtaining the observed results of a test, assuming that the null hypothesis is correct. It was calculated using the Pearson Correlation Sig-(2-tailed) test, which is a number between -1 and 1 that indicates the extent to which two variables are linearly related.

Using the absorbed doses, the equivalent doses for both ^{68}Ga -PSMA and ^{18}F -Choline were calculated. For a radionuclide permanently implanted into a patient, the dose is obtained by multiplying the initial dose rate by the half-life of the radionuclide (Menzel et al. 2015) such that:

$$D = 1.44 \times T_{1/2} \times (dD0/dt), \quad (1)$$

The type of decay for both ^{68}Ga and ^{18}F is positron emission with energies, with maximum energies of 1,899 keV for ^{68}Ga and 634 keV for ^{18}F , in addition to the emission of gamma (511 KeV). Thus, the radiation weighting factor is 1.0 (ICRP 1964).

Then the equivalent dose H_T is calculated using the following equation:

Table 1. Represents the values of ^{68}Ga -PSMA and ^{18}F -Choline dose rates between 1 m distances after 1 h along with the SUV_{max} for the kidney.

	^{68}Ga -PSMA		
	Injected activity MBq	Dose rate $\mu\text{Sv h}^{-1}$ after 1 h at 1 m	SUV_{max}
^{68}Ga-PSMA			
Minimum	84.36	14.27	2.23
Maximum	131.72	17.71	8.46
Mean	111	15.70	4.92
Standard deviation	12.21	0.87	1.62
^{18}F-Choline			
Minimum	259.00	31.61	3.08
Maximum	329.30	39.51	23.01
Mean	298.22	33.58	14.45
Standard deviation	20.35	1.72	4.35

$$H_T = \sum_R W_R D_{T,R}, \quad (2)$$

where W_R is the radiation weighting factor, which is dependent on the type and energy of the radiation R (Kendall and Smith 2002; Valentin 2002; Salame-Alfie 2008) as shown in Table 2. Graphs were drawn between the equivalent dose as a function the SUV_{max} as shown in Figs. 1 and 2.

RESULTS

Data on 80 patients with prostate cancer who had ^{68}Ga -PSMA and ^{18}F -Choline PET/CT underwent dose measurements between April 2018 and December 2018. SUV_{max} for kidneys and patients' dose rates at 1 m distance from abdomen of each patient and after 1 h measurements for both radionuclides were evaluated as shown in Table 2. The average measured exposures of ^{68}Ga -PSMA uptake with average

Table 2. Dose rate, equivalent dose and SUV_{max} for ^{68}Ga -PSMA and ^{18}F -Choline.

^{68}Ga -PSMA			^{18}F -Choline		
Dose rate $\mu\text{Sv h}^{-1}$ after 1 h at 1 m	Equivalent Dose $*10^{-6}\text{Sv}$ after 1 h at 1 m	SUV_{max}	Dose Rate $\mu\text{Sv h}^{-1}$ after 1 h at 1 m	Equivalent Dose $*10^{-6}\text{Sv}$ after 1 h at 1 m	SUV_{max}
9.41	15.3	4.17	13.00	34.24	3.08
9.64	15.69	4.79	13.00	34.24	15.04
9.75	15.87	4.95	13.00	34.24	17.45
10.18	16.57	6.73	13.00	34.24	12.96
9.39	15.28	4.11	13.99	36.87	10.06
9.99	16.25	6.16	12.00	31.61	11.29
10.08	16.41	6.36	12.00	31.61	12.31
8.77	14.27	2.23	12.00	31.61	14.04
9.53	15.51	4.46	13.00	34.24	8.62
9.30	15.13	3.78	12.00	31.61	11.66
10.11	16.45	6.61	13.00	34.24	14.18
9.01	14.67	3.26	12.00	31.61	19.93
9.78	15.91	5.01	13.00	34.24	14.52
9.82	15.98	5.76	13.00	34.24	18.5
9.15	14.89	3.52	13.00	34.24	10.67
10.88	17.71	8.46	15.00	39.51	16.4
8.95	14.56	2.68	12.00	31.61	19.51
8.92	14.52	2.59	12.00	31.61	19.47
10.48	17.06	6.91	13.00	34.24	21.41
9.36	15.24	4.08	13.00	34.24	16.58
10.00	16.28	6.51	13.00	34.24	16.74
9.68	15.75	4.83	12.00	31.63	12.14
9.16	14.91	3.53	12.00	31.61	12.39
9.79	15.93	5.34	13.00	34.24	14.54
9.51	15.47	4.45	13.00	34.24	9.95
9.48	15.42	4.35	13.00	34.24	14.83
9.52	15.49	4.45	12.00	31.61	18.37
9.28	15.10	3.65	12.00	31.61	19.78
10.87	17.69	8.35	12.00	31.61	19.68
9.81	15.97	5.55	13.00	34.24	16.47
9.66	15.72	4.83	13.00	34.24	3.75
8.90	14.49	3.03	13.00	34.24	16.04
8.79	14.31	2.27	12.00	31.64	23.01
9.32	15.16	3.84	13.00	34.24	13.37
10.21	16.62	6.81	13.00	34.24	16.26
9.57	15.57	4.61	13.00	34.24	15.74
10.10	16.43	6.51	13.00	34.24	9.88
10.72	17.45	8.19	12.00	31.61	12.38
9.28	15.11	3.69	12.00	31.61	12.81
9.80	15.95	5.52	12.00	31.61	12.19

injected radioactivity of 111 ± 0.01 MBq, after 1 h at 1 m distance, was $15.70 \pm 0.2 \mu\text{Sv h}^{-1}$ with averaged SUV_{max} of 4.92 (standard deviation = 1.62) as shown in Table 1. We noticed that there was a decrease in the dose rate at 1 m ranges between 49.3% and 51.2% compared to the dose rate at the surface (abdomen of the patient) after 1 h of ^{68}Ga -PSMA uptake, since the dose rate is decreased as the inverse square root of the distance from the source of radiation. On the other hand, the average measured exposures of ^{18}F -Choline uptake with average injected radioactivity of 298.22 ± 0.37 MBq, after 1 h at 1 m distance, was $33.38 \pm 0.2 \mu\text{Sv h}^{-1}$ with averaged SUV_{max} 14.45 (standard deviation = 4.35) as shown in Table 1. Also there was a decrease in the dose rate at 1 m ranges between 78.6% and 80.4% compared to the dose rate at the surface (abdomen of the patient) after 1 h of ^{18}F -Choline uptake. Moreover, the maximum equivalent dose for ^{68}Ga -PSMA after 1 h at 1 m distance was $17.71 \pm 0.2 \mu\text{Sv}$ with maximum SUV_{max} of 8.46 (standard deviation = 1.62). While the maximum equivalent dose for ^{18}F -Choline after 1 h at 1 m distance was $39.51 \pm 0.1 \mu\text{Sv}$ with maximum SUV_{max} of 23.01 (standard deviation = 4.35). The equivalent doses were compared to the SUV_{max} of kidney for both radionuclides as shown in Fig. 1a and b. There is positive relationship between the SUV_{max} of kidney and the ^{68}Ga -PSMA equivalent dose after 1 h of injection at 1 m distance. This relationship is statistically significant since the p-value = $0.023 < 0.05$ as shown in Table 3. By plotting the graph of the equivalent dose due to ^{68}Ga -PSMA as a function of the SUV_{max} for kidneys, we obtained a straight line of equation:

$$y = 0.5336x + 13.075, \quad (3)$$

where 0.5336 Sv is the slope of the line, and 13.075 Sv represents the y-intercept as shown in Fig. 1a. There is a

very low negative relationship between the SUV_{max} of kidney and the dose rate of ^{18}F -Choline after 1 h of injection at 1 m distance. This relationship is not statistically significant since p-value = $0.93 > 0.05$, as shown in Table 3 and in Fig. 2.

DISCUSSION

PET/CT is an imaging modality that acquires functional (PET) and anatomical (CT) information of a patient within a single examination (Brix et al. 2005; Huang et al. 2009). However, PET/CT investigations lead to exposure of patients from the internally administered PET radiopharmaceuticals and externally from x rays generated by the CT (Brix et al. 2005). The combined PET/CT examination results in an increased radiation dose to patients as compared to stand-alone components of PET/CT scan and other conventional diagnostic radiology examinations (Huang et al. 2009; UNSCEAR 2008). The effective doses from PET/CT investigations are reported to be between 13.65 and 32.18 mSv for male patients from three different PET/CT protocols (Huang et al. 2009).

There are several methods for measuring the rate and/or total amount of ^{68}Ga -PSMA and ^{18}F -Choline accumulation. The SUV is commonly used as a relative measure of ^{68}Ga and ^{18}F uptake. The use of SUVs as a measurement of relative tissue/organ uptake has been suggested as a basis for diagnosis (Kinehan and Fletcher 2010). There are large numbers of studies that discuss the SUV due to ^{68}Ga -labelled PSMA ligand (Demirci et al. 2019) and ^{18}F -Choline (Hodolic 2011). In addition, many studies discuss the SUV in normal organs (Zincirkeser et al. 2007) and in cancerous organs (Kinehan and Fletcher 2010).

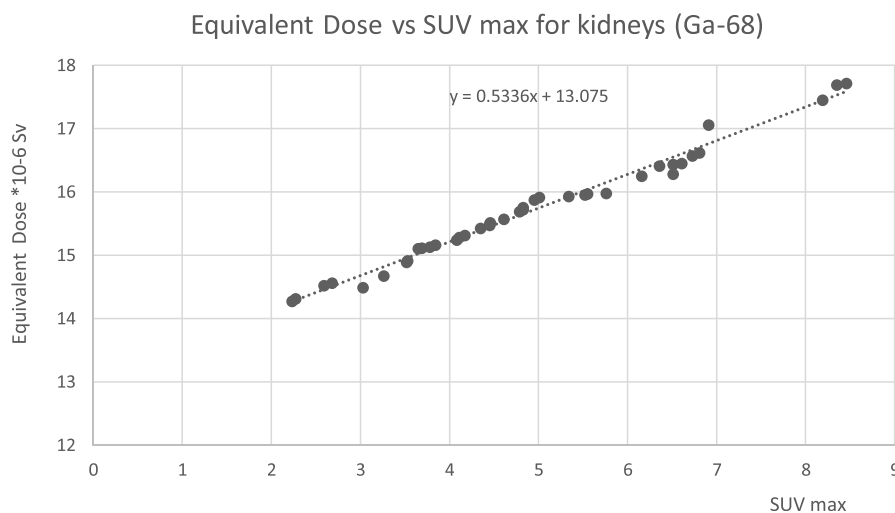


Fig. 1. The variation of equivalent dose after 1 h at 1 m as a function of SUV_{max} (kidney) for ^{68}Ga -PSMA.

Table 3. Correlation table test for doses after ⁶⁸Ga-PSMA and ¹⁸F-Choline injection.

⁶⁸ Ga-PSMA		
	Dose after 1 (h) (surface/abdomen) Pearson Correlation Sig-(2-tailed) N	SUV _{max} /kidney
Dose after 1 (h) (surface/abdomen) Pearson Correlation Sig-(2-tailed) N	1	0.271 ^a 0.023
SUV _{max} /kidney	0.271 ^a 0.023	1
	70	70
¹⁸ F-Choline		
	Dose after 1 (hr) (surface/abdomen) Pearson Correlation Sig-(2-tailed) N	SUV _{max} /kidney
Dose after 1 (h) (surface/abdomen) Pearson Correlation Sig-(2-tailed) N	1	-0.010 0.931
SUV _{max} /kidney	-0.010 0.931	1
	70	70

^aCorrelation is significant at the 0.05 level (2-tailed).

To our knowledge, this is the first study to compare the equivalent dose due to ⁶⁸Ga-labeled PSMA ligand and ¹⁸F-Choline with SUV_{max} in normal organs (kidneys). At the beginning of this study, we compared the SUV_{max} for kidneys due to ⁶⁸Ga-PSMA and ¹⁸F-Choline uptake to the mass of the patient. There was a very low positive relationship between the mass (kg) and SUV_{max} due to ⁶⁸Ga uptake ($p = 0.41 > 0.05$), and there was a very low positive relationship between the mass (kg) and SUV_{max} due to ¹⁸F uptake ($p = 0.48 > 0.05$). Thus, the relationship in both radionuclides was not statistically significant. Then we correlated the equivalent dose due to ⁶⁸Ga-PSMA and ¹⁸F-Choline with SUV_{max} for kidneys. There is a positive relationship between the SUV_{max} of kidney and the ⁶⁸Ga-PSMA equivalent dose after 1 h of injection at 1 m distance.

This relationship is statistically significant since ($p = 0.023 < 0.05$).

However, there is a very low negative relationship between the SUV_{max} of kidney and the dose rate of ¹⁸F-Choline after 1 h of injection at 1 m distance. This relationship is not statistically significant since ($p = 0.93 > 0.05$).

Thus, we can suggest in this study that the use of ⁶⁸Ga-PSMA helps in the prediction of the radiation dose when the SUV_{max} is determined from the image.

CONCLUSION

This study shows that there is positive relationship between the SUV_{max} of kidney and the ⁶⁸Ga-PSMA equivalent dose after 1 h of injection at 1 m distance. This relationship is

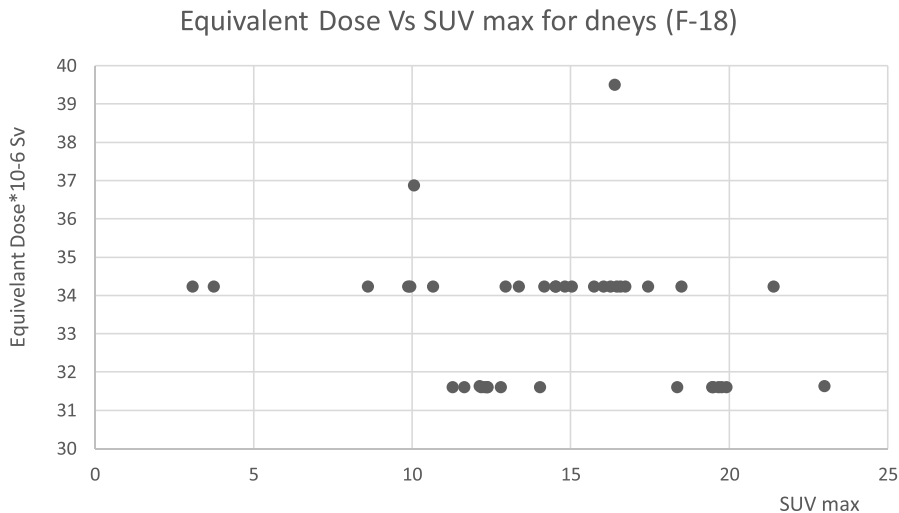


Fig. 2. The variation of equivalent dose after 1 (h) at 1 (m) as a function of SUV_{max} (kidney) for ¹⁸F-Choline.

statistically significant. However, there is a very low negative relationship between the SUV_{max} of kidney and the dose rate of ^{18}F -Choline after 1 h of injection at 1 m distance. This relationship is not statistically significant. This leads us to conclude that we can predict the radiation dose due to ^{68}Ga -PSMA for patients with prostate cancer that coincides with radiation protection principles and with the ALARA principle using the maximum standard uptake value (SUV_{max}) for the kidneys.

List of abbreviations

PET: Positron Emission Tomography
 CT: Computed Tomography
 PC: Prostate Cancer
 PSMA: Prostate-Specific Membrane Antigen
 SUV_{max} : Maximum Standard Uptake Value

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