J of Nuclear Medicine Technology, first published online October 11, 2019 as doi:10.2967/jnmt.119.233296

Development of Simple Methods to Reduce Radiation Exposure Rates to the Public from 18F-FDG PET/CT Patients

Razi Muzaffar[1], Elyse Koester[2], Sarah Frye[3], Saud Alenezi[1], Barbara B. Sterkel[4], Medhat M. Osman[1]

[1]Division of Nuclear Medicine, Department of Radiology, Saint Louis University, 3635 Vista Avenue, Saint Louis, Missouri, 63110
[2] Division of Nuclear Medicine, SSM Health St. Louis University Hospital, St. Louis, MO
[3] Medical Imaging and Radiation Therapeutics, Saint Louis University, St. Louis, MO
[4] Diagnostic Imaging Service VA, St. Louis Health Care System, Saint Louis, MO

Corresponding Author:

Medhat M. Osman

Saint Louis University

Department of Radiology/Division of Nuclear Medicine

3635 Vista Avenue, 2-DT

St. Louis, MO 63110

Telephone: 314-577-8047

Fax: 314-268-5144

medhat.osman@health.slu.edu

Word count: 2927

Financial Support: None

Key words: ALARA, PET/CT, Radiation exposure, Radiation safety

Running title: Reducing Radiation from PET/CT Patients

Abstract:

At a time when reducing the radiation dose to patients and the public has become a major focus, we assessed the radiation exposure rate from patients after an 18F-FDG PET/CT scan and evaluated different interventions to reduce it. **Methods:** 100 patients were enrolled in the study. Radiation dose rates were measured with an Ionization Survey meter after the scan in all patients. Patients were divided into 2 groups: Group 1- instructed to void then dose rates re-measured; Group 2a (pre-void)- wait 30 minutes then dose rates re-measured; Group 2b (post-void)- wait 30 minutes, void then dose rates re-measured. **Results:** 74/100 exceeded 20 μSv/h (2 mR/h) immediately after their scan. Group 1: mean dose rates decreased 20.0% from the post-scan measurement after voiding with 12/36 remaining at or above 20 μSv/h. Group 2a: mean dose rates decreased 23% from the post-scan measurement after waiting 30 minutes with 9/38 remaining at or above 20 μSv/h. Group 2b: mean dose rates decreased 35% from the post-scan measurement after waiting 30 minutes then voiding with 1/38 remaining at 20 μSv/h. **Conclusions:** Nearly 75% of patients undergoing an 18F-FDG PET/CT scan are exceeding 20 μSv/h when leaving the imaging facility. The most effective method to reduce radiation exposure was voiding after a 30 minute wait post-exam.

Introduction:

The increased utilization of diagnostic imaging throughout the world has caused a drastic increase in the radiation exposure to the population and has raised concerns for the potential cancer risks associated with the trend as well as unfavorable media coverage [1, 2]. Positron emission tomography/computed tomography (PET/CT) has emerged as the gold standard to stage and restage various types of malignancies while also seeing a steady incline in the number of studies performed. These patients are receiving radiation from the CT component of the exam but also lingering radiation from the radiopharmaceutical 18F-fluoro-deoxyglucose (18F-FDG). Both nuclear medicine and PET/CT studies inherently have additional radiation exposure to the general public compared to CT and X-ray due to the administration of radiopharmaceuticals. This concern has led to various new techniques and has paved the way for technological advancements to both improve image quality while at the same time reducing the amount of radiation a patient is exposed to.

The Nuclear Regulatory Committee (NRC) has well-established guidelines for the release of patients undergoing therapeutic procedures [3]. The maximum accepted exposure to the public from a material source is 20 μSv/h (2 mR/h) and is used as a benchmark to reduce exposures to As Low As Reasonably Achievable (ALARA) [4]. However, guidelines addressing the release of a patient undergoing diagnostic nuclear medicine or PET/CT exams are not as clear. Nevertheless, medical facilities are under increased scrutiny to reduce radiation exposure to both patients and the public.

Although the half-life of 18F-FDG is relatively short (110 minutes), many patients have multiple tests and clinical appointments in a single visit, so it is important to consider the

timeframe immediately after a scan. At a time when reducing the radiation dose to patients and imaging staff has become a major focus, this study set out to explore the effectiveness of reducing the radiation exposure to the public from a patient who received a standard of care 18F-FDG PET/CT exam. We sought a low-cost solution with the least impact or inconvenience to the patient and the PET/CT department. In addition, renal function was evaluated as a potential variable to impact this exposure. As proof of principle, we also evaluated the radiation exposure from a small group of patients undergoing 18F-Fluciclovine PET/CT studies due to the difference in imaging time of 3-5 minutes post-injection compared to the 60 minutes for 18F-FDG .

Materials and Methods:

Patients undergoing standard of care 18F-FDG PET/CT exams who were willing to be included in our measurements were enrolled in the study for a total of 100 patients (61 M: 39 F; mean age 54). The patients received a weight based 18F-FDG dose (range: 233.1 MBq - 558.7 MBq (6.3 mCi - 15.1 mCi), mean: 421.8 MBq (11.4 mCi)) followed by an approximate 60 min uptake time (total uptake time: 51-93 minutes, mean 62 minutes). They were then instructed to void immediately prior to a standard of care whole body PET/CT acquisition (total image acquisition time: 14-47 minutes, mean 26 minutes). Each patient was then measured with an Ionization Survey meter (Victoreen Ion Chamber Survey meter model 450) for radiation dose rates at 1 meter after the PET/CT exam. A dedicated area was used for measurement at 1 meter to ensure consistency. All measurements were performed by the same technologist with the survey meter aimed at the bladder. Patients were randomly divided into 2 groups based upon availability after the PET/CT exam. All patient dose rates were measured immediately after the PET/CT exam. Group 1 (n=50) patients were instructed to void and their dose rates were re-

measured. Group 2a (pre-void; n=50) patients waited 30 minutes after the PET/CT exam and dose rates were measured. These patients were then instructed to void and dose rates were re-measured (Group 2b post-void). Consideration of renal function was also investigated with 77/100 patients having renal function data and estimated glomerular filtration rate (eGFR) values within 2 weeks of the scan.

A small sample of 12 male patients (mean age 62) undergoing standard of care 18F-Fluciclovine PET/CT for prostate cancer with biochemical recurrence were also evaluated. Although the F-18 dose is comparable, the difference in protocol between the 18F-Fluciclovine and FDG patients was assessed (3-5 mins vs. 60 mins). All patients received the standard 370 MBq (10 mCi) dose and images were acquired 3-5 minutes after radiotracer administration. Upon completion of imaging, each patient was measured with the same Ionization Survey meter for radiation dose rates at 1 meter. Patients were instructed to wait 30 minutes and dose rates were re-measured. Each patient was then instructed to void and the final dose rates were measured. This project was undertaken as a Quality Improvement initiative. The Institutional Review Board reviewed this study and determined it did not need approval under their guidelines.

Results:

In total, 74/100 patients (74%) exceeded 20 μSv/h (2 mR/h) at 1 meter immediately after their PET/CT scan. Of these, 36/74 (49%) were from Group 1 and 38/74 (51%) from Groups 2a (pre-void) and 2b (post-void). The findings after the different interventions were as follows: Group 1: mean exposure from patients decreased by 20% (23 μSv/h to 18.3 μSv/h) after voiding but 12/36 (33%) remained at or above the 20 μSv/h threshold. Group 2a (pre-void): mean

exposures decreased by 23% (23.4 μSv/h to 18 μSv/h) after waiting 30 minutes but 9/38 (24%) remained at or above the 20 μSv/h threshold. Group 2b (post-void): mean exposures decreased by 35% from the post-scan measurement (23.4 μSv/h to 15.1 μSv/h) with only 1/38 (3%) remaining at the 20 μSv/h threshold (Figure 1).

Of the 77 patients with renal function data, only 12/77 (16%) had reduced renal function (eGFR <60). Of these, 11/12 (92%) were above the 20 μSv/h immediately after the scan, whereas 47/65 (72%) of normal eGFR patients were above 20 μSv/h after the scan (Figure 2). The data suggests patients with reduced renal function have higher radiation exposure compared to those with normal renal function. However, this was found to be not statistically significant in this study with a p-value of 0.274.

Of the 12 patients undergoing 18F-Fluciclovine PET/CT, 12/12 (100%) remained at or exceeding the 20 μSv/h threshold immediately after the scan. Upon waiting 30 minutes, the mean exposures decreased by 25% (28.2 μSv/h to 21.2 μSv/h) but 9/12 (75%) remained at or exceeding the 20 μSv/h threshold. Upon waiting 30 minutes plus voiding, the mean exposures decreased by 30% (28.2 μSv/h to 19.8 μSv/h) but 9/12 (75%) continued to be at or exceeding the 20 μSv/h threshold. When comparing the most effective intervention of waiting 30 minutes plus voiding between the 18F-FDG and 18F-Fluciclovine studies, we found that 97% (37/38) of the 18F-FDG patients who initially exceeded the 20 μSv/h radiation exposure fell below the threshold compared to only 25% (3/12) of the 18F-Fluciclovine patients (Figure 3).

Discussion:

The ever expanding use of diagnostic imaging continues to raise concerns related to the increased cancer risk from ionizing radiation exposure. This has been especially critical for

children and young adults. Multiple media reports have surfaced describing the increased cancer risk from medical imaging exams. During this same period, the use of diagnostic imaging has been increasing at a steady pace. While the natural background radiation has not significantly changed, the radiation exposure from medical imaging has increased more than 6-fold. According to a report issued in March 2009 by the National Council on Radiation Protection and Measurements, medical imaging contributed to about 15% of the overall radiation dose in the US in the 1980's compared to about 50% in 2006 [5]. The utilization of PET/CT in the clinical setting has also been expanding with the advancement in medicine and technology. The number of PET/CT systems increased over 10-fold since 2001 and the number of clinical scans performed in the US alone is estimated at nearly 2 million which is an increase of 13% compared to 2015 [6, 7].

The concerns of public exposure to ionization radiation from medical imaging have brought about a movement in both the pediatric population with the Image Gently campaign and the adult population with the Image Wisely campaign. In order to maximize the risk-to-benefit ratio, the medical community attempts to optimize diagnostic image quality while at the same time following the ALARA principles. The Image Gently and Image Wisely campaigns were developed to educate both providers and consumers in an attempt to curtail unnecessary imaging and reduce radiation exposure [8-10]. However, there continues to be a debate whether low-dose radiation exposure can cause cancer [11]. In a recent publication, Siegel et al have made the case for terminating these campaigns due to the erroneous extrapolation of the linear no-threshold model from high- to low-dose radiation as well as propagating radiophobia. The linear no-threshold (LNT) model for radiation-induced cancer has guided radiation protection policies since the 1950s and supported by national and international advisory bodies. It is based on the

concept that low levels of radiation increases mutations which leads to increased cancers. However, Siegel et al claim low-dose radiation may even help prevent cancer by inducing repair of preexisting and ongoing DNA damage while repairing radiogenic damage [12-15]. Nevertheless, from the regulatory standpoint, the LNT model is accepted and continues to be supported by national advisory bodies (National Research Council and National Council on Radiation Protection and Measurements) [16,17]. Furthermore, those questioning the LNT model are basing the risk versus benefit only for the patient. This point of view should not be the same for the general public or potentially vulnerable patient populations in hospital or clinic waiting areas. It has been shown that the cancer risk increases substantially in patients with a suppressed immune system such as in young AIDS patients where the cancer incidence increases by a factor of 40 or in young organ transplant patients where the cancer mortality rate increases by a factor of 60 [18,19]. Nonetheless, a balance needs to be made between radiation risks versus radiation aversion.

Various techniques have been developed to decrease the amount of radiation exposure by using weight-based-protocols for both the radiopharmaceutical delivered and the CT. Furthermore, PET/CT systems with higher sensitivity and improved performance can take advantage of enhanced detector technology (better time-of-flight performance, continuous bed motion or extended axial field of view) to reduce the 18F-FDG dose [20, 21]. According to the Society of Nuclear Medicine and Molecular Imaging guidelines, the typical administered 18F-FDG dose is 370-740 MBq (10-20 mCi) [22]. However, patients who weigh >75 kg should receive a slightly higher dose in order to compensate for degraded image quality due to a lower signal to noise ratio from excessive attenuation [20].

While these advancements and techniques address the radiation exposure to patients and radiation workers, they do not address the exposure from patients to the public and repeated exposure to unmonitored non-radiologic medical staff. Many patients schedule multiple tests and clinical appointments in a single day which not only exposes other patients in waiting areas but also general medical personnel. Multiple studies have been performed to assess the amount of radiation received by medical personnel in various roles [23]. Regardless of the validity of the LNT model, there is a justification for the radiation exposure for both patients and radiation workers, however, the same cannot be said for the general public.

Our study evaluated simple non-invasive interventions to reduce the overall radiation exposure to the public with no additional cost and only an additional 30 minutes for the patient. At a time when the NRC has strict guidelines regarding the release of a patient treated with a radioisotope, the recommendations about releasing a patient undergoing a diagnostic PET/CT are not as clear. In addition, national and international guidelines (Society of Nuclear Medicine and Molecular Imaging, American College of Radiology, European Association of Nuclear Medicine) neither give recommendations for radiation exposure from patients nor recommends voiding or waiting after a scan prior to release [20, 22, 24]. Although our data regarding the reduced radiation exposure after voiding was similar to prior studies, we found nearly 75% of patients undergoing an 18F-FDG PET/CT scan leave the imaging facility exceeding 20 μSv/h at 1 meter [25]. We also attempted to address the concern of reduced renal function in these patients. Although renal failure has been shown not to have a significant impact on the 18F-FDG biodistribution in PET/CT, our initial data shows a possible correlation with impaired renal function and elevated radiation exposure [26]. However, due to our small sample size this was not found to be statistically significant.

Moreover, the initial data from patients undergoing a 18F-Fluciclovine study exhibited a higher radiation exposure to the public than those undergoing an 18F-FDG study. The higher exposure is most likely due to the elimination of the 60 minute uptake phase given the different pharmacodynamics. Sorensen et al demonstrated that tumor uptake with 18F-Fluciclovine peaks around 3 minutes with a plateau from 3-12 minutes and gradual washout. Lymph node uptake was rapid with an even faster washout than tumor, and the urinary bladder had gradual uptake [27]. Therefore, standard imaging with 18F-Fluciclovine is performed 3-5 minutes after radiotracer administration compared to 60 minutes with 18F-FDG [28]. Although the Fluorine-18 isotope is the same in both the 18F-Fluciclovine and 18F-FDG studies as well as a similar injected dose of 370 MBq vs 421.8 MBq (10 mCi vs 11.4 mCi), the difference in protocol with 18F-Fluciclovine requires a significantly shorter uptake phase. In our study, this difference resulted in 75% of the 18F-Fluciclovine patients remaining above the 20 μSv/h threshold after waiting 30 minutes plus voiding versus only 3% for the 18F-FDG patients.

To the best of our knowledge, this study may be the first to evaluate the radiation exposure to the public from a patient undergoing an 18F-FDG PET/CT scan and assess the feasibility of implementing simple interventions to significantly reduce the radiation exposure to the public. Other studies have addressed radiation exposure but in the context of exposure to a patient or technologists [25, 29]. In addition, the effects of voiding after imaging to reduce exposure has also been studied but not the combination of waiting plus voiding. In theory, these principles can also be utilized for other diagnostic PET and nuclear medicine studies prior to a patient leaving an imaging facility.

Our study is not without limitations. The relatively small sample size limits the statistical significance of the findings, especially when evaluating the effect of renal impairment. A larger

sample size could allow for evaluation of various stages and severity of renal disease. Additionally, only 12 patients undergoing an 18F-Fluciclovine study were evaluated. Other commonly used FDA approved PET tracers such as 18F-Sodium Fluoride and Ga-68 dotatate should also be evaluated. We found even the same isotope can have vastly different radiation exposures to the public depending on protocol. Lastly, this study was limited to the experience of a single institution with a fixed scanner. Due to financial concerns, a fixed PET/CT scanner is not always cost-effective and often a mobile PET/CT scanner is utilized. However, given the space and time constraints of a mobile scanner, these simple interventions may not be feasible. A prospective multi-institute study would be able to better assess various patient populations, different radiotracers, different protocols, and comparing both fixed and mobile facilities.

Conclusion:

Current guidelines do not advocate measuring radiation exposure from patients undergoing 18F-FDG PET/CT studies prior to release from an imaging facility. Our analysis shows radiation exposure from nearly 75% of patients undergoing an 18F-FDG PET/CT exam are exceeding 20 μSv/h when leaving the imaging facility and all patients undergoing 18F-Flucicolvine PET/CT exceed this amount. The most effective method to reduce radiation exposure from the 18F-FDG patients to under 20 μSv/h was voiding after a 30 minute wait post-exam with 97% of patients below the 20 μSv/h threshold. This simple intervention is especially important when patients have additional appointments and are in close contact with others. However, this was not as effective in the 18F-Fluciclovine patients resulting in only 25% of patients below the threshold. Therefore, more effective techniques should be developed and validated in order to reduce the radiation exposure from patients undergoing non-18F-FDG PET/CT scans.

References:

1. Morin RL, Seibert JA, Boone JM. Radiation Dose and Safety: Informatics Standards and Tools. J Am Coll Radiol. 2014 Dec;11(12 Pt B):1286-97.

2. Berrington de Gonzalez A, Mahesh M, Kim K-P, et al. Projected cancer risks from computed tomographic scans performed in the United States in 2007. Arch Intern Med 2009;169:2071-7.

3. "35.75 Release of individuals containing unsealed byproduct material or implants containing byproduct material." United States Nuclear Regulatory Commission. Accessed September 6, 2018. http://www.nrc.gov/reading-rm/doc-collections/cfr/part035/part035-0075.html

4. Howe D.B., Beardsly M, Basksh S. Consolidated Guidance about Materials Licenses: Program-Specific Guidance about Medical Use Licenses Final Report. United States Nuclear Regulatory Commission. Jan 2008. NUREG-1556. Vol. 9, Rev.2.

5. Bolus NE. NCRP report 160 and what it means for medical imaging and nuclear medicine. J Nucl Med Technol. 2013 Dec;41(4):255-60.

6. 2011 PET Imaging Market Summary Report. Greenbelt, MD: IMV; 2011.

7. "PET Imaging Market Summary Report 2018." IMV Medical Information Division. Accessed September 11, 2018. http://imvinfo.com/product/pet-imaging-market-summary-report-2018/

8. Brink J, Amis ES. Image Wisely: A Campaign to Increase Awareness about Adult Radiation Protection. Radiology. 2010 Dec;257(3):601-2.

9. Goske MJ, Applegate KE, Boylan J, et al. The Image Gently campaign: working together to change practice. AJR Am J Roentgenol. 2008 Feb;190(2):273-4.
m
10. Cohen MD. ALARA, Image gently and CT-induced cancer. Pediatr Radiol. 2015 Apr;45(4):465-70.

11. Doss, M. Are We Approaching the End of the Linear No-Threshold Era? J Nucl Med. 2018 Dec;59(12):1786-1793.

12. Siegel JA, Sacks B, Pennington CW, et al. Dose Optimization to Minimize Radiation Risk for Children Undergoing CT and Nuclear Medicine Imaging Is Misguided and Detrimental. J Nucl Med. 2017 Jun;58(6):865-868.

13. Siegel JA, Pennington CW, Sacks B. Subjecting Radiologic Imaging to the Linear No-Threshold Hypothesis: A Non Sequitur of Non-Trivial Proportion. J Nucl Med. 2017

Sep;58(9):1529-1530.

14. Duncan JR, Lieber MR, Adachi N, et al. DNA Repair After Exposure to Ionizing Radiation Is Not Error-Free. J Nucl Med. 2018 Feb;59(2):348.

15. Siegel JA, Sacks B, Pennington CW, et al. Reply: DNA Repair After Exposure to Ionizing Radiation Is Not Error-Free. J Nucl Med. 2018 Feb;59(2):349.

16. National Research Council of the National Academies. Health Risks from Exposure to Low Levels of Ionizing Radiation: BEIR VII Phase 2. Washington, DC: The National Academies Press; 2006:424.

17. NCRP. Commentary No. 27: Implications of Recent Epidemiologic Studies for the Linear-Nonthreshold Model and Radiation Protection. Bethesda, MD: National Council on Radiation Protection and Measurements; 2018:210.

18. Oliveira Cobucci RN, Saconato H, Lima PH, et al. Comparative incidence of cancer in HIV-AIDS patients and transplant recipients. Cancer Epidemiol. 2012 Apr;36(2):e69-73.

19. Biggar RJ, Frisch M, Goedert JJ; AIDS-Cancer Match Registry Study Group. Risk of cancer in children with AIDS. JAMA. 2000;284:205–209.

20. Boellaard R, Delgado-Bolton R, Oyen WJ, et al. FDG PET/CT: EANM procedure guidelines for tumour imaging: version 2.0. Eur J Nucl Med Mol Imaging. 2015 Feb;42(2):328-54.

21. Murray I, Kalemis A, Glennon J, et al. Time-of-flight PET/CT using low-activity protocols: potential implications for cancer therapy monitoring. Eur J Nucl Med Mol Imaging. 2010 Aug;37(9):1643-53.

22. Jadvar H, Colletti PM, Delgado-Bolton R, et al. Appropriate Use Criteria for 18F-FDG PET/CT in Restaging and Treatment Response Assessment of Malignant Disease. J Nucl Med. 2017 Dec;58(12):2026-2037.

23. Kitahara CM, Linet MS, Balter S, et al. Occupational Radiation Exposure and Deaths From Malignant Intracranial Neoplasms of the Brain and CNS in U.S. Radiologic Technologists, 1983-2012. AJR Am J Roentgenol. 2017 Jun;208(6):1278-1284.

24. "ACR–SPR Practice Parameter for performing FDG-PET/CT in Oncology." American College of Radiology. Accessed January 8, 2019. https://www.acr.org/-/media/ACR/Files/Practice-Parameters/fdg-pet-ct.pdf

25. Madsen MT, Anderson JA, Halama JR, et al. AAPM Task Group 108: PET and PET/CT shielding requirements. Med Phys. 2006 Jan;33(1):4-15.

26. Kode V, Karsch H, Osman MM, et al. Impact of renal failure on F-18-FDG PET/CT scans. Front Oncol. 2017; 7: 155.

27. Sörensen J, Owenius R, Lax M, et al. Regional distribution and kinetics of [18F]fluciclovine (anti-[18F]FACBC), a tracer of amino acid transport, in subjects with primary prostate cancer. Eur J Nucl Med Mol Imaging. 2013 Feb;40(3):394-402.

28. Axumin Fluciclovine F18 Injection. Accessed September 21, 2018. www.axumin.com

29. Bayram T, Yilmaz AH, Demir M, et al. Radiation dose to technologists per nuclear medicine examination and estimation of annual dose. J Nucl Med Technol. 2011 Mar;39(1):55-9.

Figure 1. Comparison of patients above the 20 µSv/h threshold measured immediately after the PET/CT scan (Blue) vs. patients above the 20 µSv/h threshold after various interventions to reduce the radiation exposure (Red).

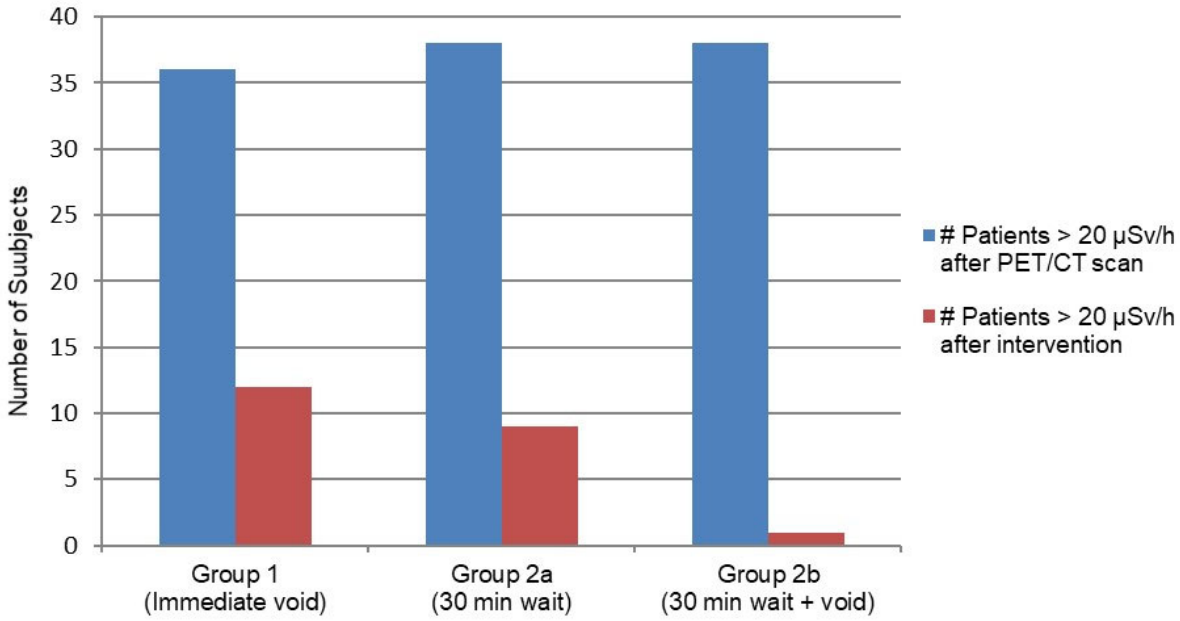

Figure 2. Comparison of patients with normal eGFR vs. patients with abnormal eGFR. The green bar depicts the number of patients total in each group based of eGFR. The yellow bar depicts the number of patients with elevated radiation exposure levels above 20 µSv/h immediately after imaging.

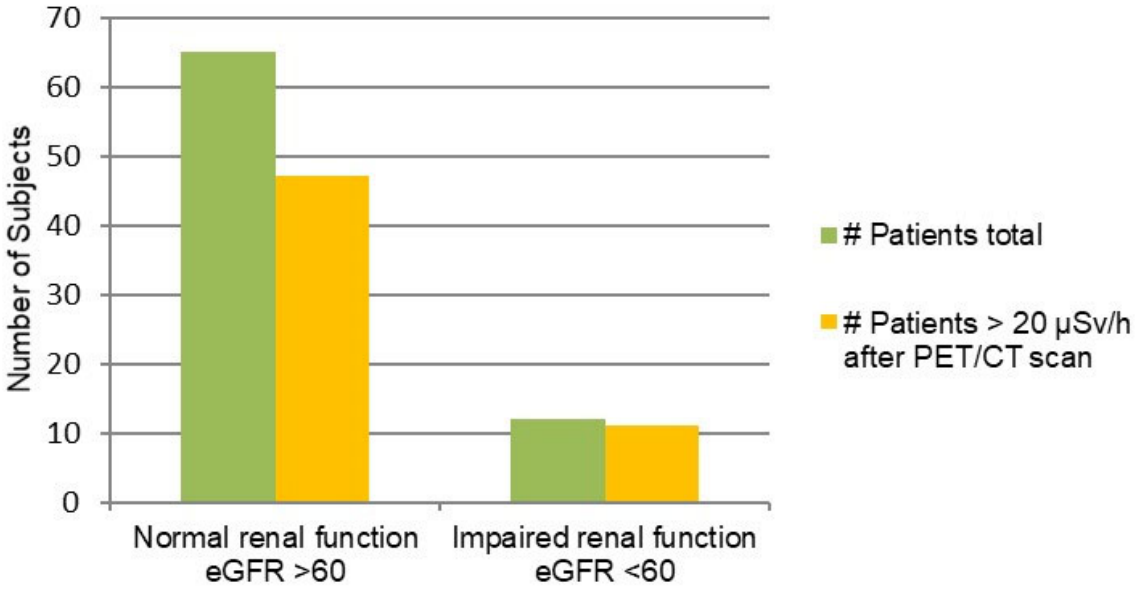

Figure 3. Comparison of radiation exposure from patients undergoing 18F-FDG PET/CT scan versus 18F-Fluciclovine PET/CT scan. The blue bar depicts the number of patients exceeding 20 µSv/h immediately after the scan and the red bar depicts the number of patients which continue to exceed 20 µSv/h after waiting 30 minutes and voiding after the scan.