Patients Undergoing Multiple ^{18}F -FDG PET/CT Scans: 11-Year Study At A High-Capacity Center

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Abstract

Purpose

To assess frequency, clinical indications, and cumulative effective dose (CED) of patients undergoing multiple ^{18}F -FDG PET/CT imaging.

Methods

Retrospective analysis of ^{18}F -FDG PET/CT scans performed at a University hospital for 11 years was done. Effective dose was computed from activity administered and dose-length-product.

Results

A total of 55,424 ^{18}F -FDG PET/CT scans were performed in 32,658 patients. The average injected activity was 421 MBq and median 417 MBq. 24.2% of the patients were scanned 2-5 times in a year, 16.7% of them being unique patients (not counted as separate patient in different years). The maximum PET/CT scans in a year was five. 23571 (72.2 %) patients underwent a single ^{18}F -FDG PET/CT scan, while 9087 (27.8%) unique patients underwent 2 - 23 scans during 11 years. 82% of the scanned patients had malignant disease, 2.4% among the patients with ≥ 2 ^{18}F -FDG PET/CT scans in a year were with non-malignant indications. 1.4% of patients received CED ≥ 100 mSv in one year from multiple ^{18}F -FDG PET/CT scans and 0.8% of them received ≥ 100 mSv in a year more than one time, the CED of 27.8% (9087 patients) who underwent 2 to 23 ^{18}F -FDG PET/CT scans over 11-years ranged from 38 to 575 mSv (median: 271 mSv).

Conclusion

This first and largest ever study covering analysis of 11-years' data of ^{18}F -FDG PET/CT patients showed that a sizeable number of patients, largely (82%) with malignant disease undergo recurrent imaging during one year and non-ignorable fraction exceed 100 mSv in one year.

Introduction

^{18}F Fluorine-fluorodeoxyglucose (^{18}F -FDG) is regarded as the most common radiopharmaceutical used in positron emission tomography/computed tomography (PET/CT) for cancer staging and re-staging, estimating prognosis, assessment of therapy response, and follow-up. ^{18}F -FDG also played a key role in the imaging and diagnosis of some neuropsychiatric and cardiac conditions as well as inflammation and infection disorders [1, 2, 3]. FDG is an analogous agent to the vital glucose and therefore the amount of FDG consumed or taken up by the cells expresses the respective metabolic status.

PET/CT is a hybrid imaging modality that enables simultaneous display and coregistration of CT and PET images providing concurrent morphologic and physiologic information [4, 5]. The body coverage or scan length can be changed with respect to the clinical indication, types of tumor, and suspected sites of extension. In general, there is whole-body imaging mode encompassing the top of the head to the feet (standard for both Europe and the US), while torso-imaging mode involves the base of the skull to mid-thigh covering most of the relevant regions of the body (standard for both Europe and the US) [6, 7]. In certain cases, a cranially extended torso imaging route may be also applied to cover the brain in the same scan (from the top of the head to mid-thigh). The typical injected activity is dependent on many factors including the acquisition speed, PET scanner sensitivity, and the common national regulatory. However, the EANM guidelines elaborated two recommendations for determining the minimum FDG administered dose in adults through a linear and a quadratic relationship between PET acquisition time per bed position, patient weight, and recommended FDG activity [7]. For the CT component, it is allowed to adjust the exposure parameters according to the indications or the desirable clinical needs. In common practice, a low-dose CT protocol is majorly accepted for attenuation correction and anatomic localization, however, the exposure factors are higher (more x-ray burden) when a diagnostic CT image with greater details is required either with contrast enhancement or contrast free. Regardless of the acquisition fashion, the radiation dose arising from PET/CT scans has been a matter of concern [8, 9].

At the moment it is not known how often a patient undergoes ^{18}F -FDG PET/CT exams, the age distribution of patients who undergo multiple exams, their diagnoses, and cumulative radiation doses involved.

To this end, the main focus of the present study is to track the frequency of ^{18}F -FDG PET/CT scans for a population of patients with different disease conditions over 11 years.

Methodology

Medical records of patients subjected to ^{18}F -FDG PET/CT scan at Istanbul University- Cerrahpasa, Cerrahpasa Hospital Turkey were retrospectively analyzed for nearly 11 years from 04 Jan 2010 to 04 Nov 2020. This retrospective study was approved by the ethical committee of the institute at Cerrahpasa medical school. In our site, parameters of patients undergoing ^{18}F -FDG administration like patients name, ID, indications, administered activity, date, and time of administration are available through the archiving system.

PET/CT scans were routinely acquired with cranially extended torso imaging protocol from top of head to mid-thigh following ^{18}F -FDG administration. However, some pathologic conditions exclusively necessitate full-body scan like melanoma, bone cancer or metastases and inflammatory diseases. Two types of PET/CT systems are available in the department and were used. First, Siemens biograph 6 with $6.4 \times 6.4 \times 25 \text{ mm}^3$ LSO scintillators integrated to 6 slices rotating CT scanner. The computed tomography (CT) scans were carried out using 130 kVp, tube current modulation ranging from ≈ 35 -290 mA across the axial sections, 4 mm slice thickness, 0.921sec rotation time. The second PET/CT scanner (GE discovery

710) has been installed since early 2014 with 4.2 x 6.2 x 30 mm³ LYSO crystals and 585 ps coincidence timing. The CT scans were done using helical mode with 16 detectors rows. The imaging settings were: 120 kVp, tube current modulation typically with 35-215 mA, 0.7 sec rotation time, 18.8 mm table feed per rotation, 16x1.25 mm collimation width, and 0.938 pitch limit. Since 2014, GE scanner has become a workhorse making up 96 % of the performed PET/CT scans until the end of 2020.

Patients who were scanned multiple times at Cerrahpaşa hospital in a year were identified from patient ID. This helped to identify patients who were scanned frequently. The maximum number of scans made during every 1 year period for any patient was assessed by counting the number of repeated ID's in a given year.

A set of commands was used in an excel sheet to extract the number of patients who were repeatedly scanned year by year among thousands of patients enrolled for ¹⁸F-FDG PET/CT over the study period. In addition to studying the frequency of patients undergoing multiple PET/CTs, we estimated the total number of scans for all patients who had more than one scan in any year.

The effective dose (E) from ¹⁸F-FDG was estimated using the dose conversion coefficient of 0.019 mSv/MBq as provided by ICRP Publication 128 [10].

For estimation of E from CT scans, the region-specific conversion coefficients (CFs) from dose length product (DLP) to E were summerized by Deak and co-authors [11]. The CF at 120 kVp was reported to be 0.0019, 0.0051, 0.0145, 0.0153 and 0.0129 for head, neck, chest, abdomen, and pelvis, respectively. Whereas, the corresponding CFs at 140 kVp were 0.0019, 0.0052, 0.0147, and 0.0155. Since the scan length of whole body PET/CT encompasses all of the above mentioned regions and 120 kVp was used for GE Discovery scanner, the average of the conversion coefficients for chest, abdomen and pelvis were used to estimate the E for patients scanned on GE discovery 710. Similarly, for Siemens PET/CT with 130 kVp, the average of the corresponding conversion coefficients was used. For head and neck, the corresponding coefficients were used assuming 15 cm and 12 cm scan length, respectively. The total scan length was set as 120 cm.

In accordance with the earlier assumptions, the formula below was used to estimate the total E from multiple ¹⁸F-FDG PET/CT scans:

Total E= E from PET part + E from CT part

Total E = [n × A (MBq) × 0.019 (mGy/MBq)] + [n × CF × DLP]

E: effective dose, n: number of scans, A: administered ¹⁸F-FDG activity, CF: conversion factor, DLP: dose linear product (mGy.cm²).

Results

During the observation period of ≈ 11 years, the total number of the performed ^{18}F -FDG PET/CT scans was 55,424 in 32,658 patients. The average activity injected was 334 ± 86 MBq in GE and 507 ± 118 MBq in Siemens. The average injected activity to all population was found to be 421 MBq and the median value was 417 MBq. As addressed in Table 1, a total of 7898 (24.2 %) patients involving 4897 females (15.0%) and 3001 (9.2%) males were scanned ≥ 2 times in a year during the 11 years. This number is the sum of the patients with 2-5 scans in a year counted year by year separately (sum of 2010, 2011...2020) without pooling. Around 5430 (16.6 %) of them underwent ^{18}F -FDG PET/CT scan twice in a year, and 1952 (6 %) patients were scanned three times in a year. Whereas, the patients with 4 and 5 scans in a year were less frequent as 488 patients (1.5 %) and 28 patients (0.1 %), respectively.

Table 1

Gender identity of the patients who underwent ≥ 2 ^{18}F -FDG- PET/CT scans in a year

No. of ^{18}F -FDG PET/CT scans	Female	Male	Total
2	3358 (10.3%)	2072 (6.3%)	5430 (16.6%)
3	1210 (3.7%)	742 (2.3%)	1952 (6%)
4	312 (1%)	16 (0.5%)	488 (1.5%)
5	17 (0.1%)	11 (0.03%)	28 (0.1%)
	4897 (15.0%)	3001 (9.2%)	7898 (24.2%)

Figure 1 also depicts the year-wise distribution of the number of patients who received 2,3,4 or 5 ^{18}F -FDG scans in any individual year. No patient was scanned with ^{18}F -FDG more than 5 times in a year.

When the patients with 2-5 scans in a year were pooled together as shown in Table 2, 2442 (7.4%) out of 7898 patients were found duplicated and the absolute patients' number decreased to 5456 (16.7%) by counting the unique IDs only.

Table 2

Total number of patients with ≥ 2 scans in a year counted separately and uniquely.

scans in a year	Total # of patients	# of Unique patients
2	5430 (16.6%)	4092(12.5%)
3	1952 (6%)	1123(3.4%)
4	488 (1.5%)	225(0.69%)
5	28 (0.1%)	16(0.049%)
Total	7898 (24.2%)	5456 (16.7%)

When consolidated over the entire period of about 11 years, the total number of scans ranged between 1-23 for the patients population as illustrated in figure 2. Thus, a large group of patients with several scans over 11 years were repetitively counted within those with 2-5 scans in a year and also numerous patients had only 1-5 scans over 11 years that all made in a single year. In more elaboration, Table 3 comprehensively demonstrated all the patients who scanned 2- 23 times over 11 years as function of 1,2,3,4 and 5 scans in a year showing both the unique and duplicated subjects. For example, 13045 patients were counted with a single scan in a year during 11 years (with ≥ 2 scans over 11 years), however, the absolute number of those patients was 6521 (19.9%) after ignoring the repeated IDs (6524 subjects) along the years. Likewise, 5430 patients were counted with 2 scans in a year during 11 years, while the number of the patients was merely 4450 (13.6%) and the remaining 980 were repeated subjects. In contrast, the 28 (0.085%) patients with 5 scans in a year were totally different individuals.

Furthermore, the patients shown in figure 2 were pooled together and it was explicated that 9087 (27.8%) unique patients underwent 2 to 23 scans during 11 years. Among them, 6513 (72%) were scanned with GE and the remaining 2574 (28 %) patients with Siemens.

Table 3
Total number Patients with 2-23 ¹⁸F-FDG PET/CT scans over 11 years filtered by scans in a year involving unique and duplicated subjects.

Scans in a year	Total # of patients with sc-y over 11 years	# of unique patients with sc-y over 11 years	# of duplicated patients with sc-y over 11 years
1	13045	6521	6524
2	5430	4450	980
3	1952	1529	423
4	488	435	53
5	28	28	0

The medical indication for ¹⁸F-FDG imaging in 82 % of the patients was malignant diseases. Other conditions and their frequency were: 5% inflammatory diseases, 2% cardiac, 2% neural conditions and the remaining 9% for tumor survey and other conditions as illustrated in figure 3. 2.4% of the patients with ≥ 2 ¹⁸F-FDG PET/CT scans in a year were with non-malignant indications, and likewise 3% of those scanned ≥ 2 times over 11 years.

The average CTIvol was learned from the dose reports obtained at the end of the scan for group of patients. The mean 32-cm CTIvol in GE was 12.4 mGy, while that was 6.3 mGy in Siemens applied on the region from chest to femur. The mean 16-cm CTIvol for Siemens was learned from brain PET/CT scans

as 13.2 mGy, while the 16-cm CTIvol of GE was missed in the dose reports and therefore it was assumed 2 × 32-cm CTIvol. The 16-cm CTIvol was applied on the head and neck.

Consequently, the average effective dose to an individual patient following a single ¹⁸F-FDG PET/CT scan was estimated as 25.0 mSv from GE and 19.2 mSv from Siemens that translates further to those with higher number of scans as shown in table 4. Overall, 446 patients (1.4 %) received a total effective dose above 100 mSv in one year from multiple ¹⁸F-FDG PET/CT scans. Among them, 260 (0.8 %) patients received ≥ 100 mSv in a year more than one time as they underwent more than 8 scans over 11 years. Furthermore, the cumulative effective dose (CED) of 9087 (27.8%) patients who underwent 2 to 23 ¹⁸F-FDG PET/CT scans over 11 years was ranging from 38 to 575 mSv (median: 271 mSv). Among them, 2415 patients (27 %) had CED above 100 mSv during 11 years and the rest 6331 patients (73 %) showed CED below 100 mSv.

Table 4 The estimated total effective TE dose of individual patient from ¹⁸F-FDG PET/CT scans

¹⁸ F-FDG scans	TE dose (mSv)	
	GE	Si
2	50	39
3	75	58
4	100	77
5	125	96

Discussion

The important findings of this 11-year study covering 55,424 ¹⁸FDG-PET/CT exams in 32,658 patients include 24.2% patients scanned 2-5 times in a year, 16.7% of them being unique patients (not counted a separate patient in multiple years), the maximum PET/CT scans in a year of 5, 82% of this patient cohort having malignant disease, 2.4% of the patients with ≥ 2 ¹⁸F-FDG PET/CT scans in a year were with non-malignant indications, 1.4% patients received a total effective dose above 100 mSv in one year from multiple ¹⁸F -FDG PET/CT scans and 0.8% of them received ≥ 100 mSv in a year more than one time, the CED of 27.8% (9087 patients) who underwent 2 to 23 ¹⁸F -FDG PET/CT scans over 11 years ranged 38 to 575 mSv (median: 271 mSv).

This comprehensive study is first of its kind, to the best of our knowledge, and that too from a country where tools for radiation dose assessment such as commercial dose management systems are hardly available. In Turkey, there were about 1.67 active PET/CT scanners per 1 000 000 populations in 2019 according to OECD publication [12]. Also, the PET/CT frequency in Turkey was 4.2 scans per 1000 population less than the average frequency of the other 37 countries in the OECD with 4.39 scans per 1000 population [12]. However, according to information from Siemens/Turkey branch, it was revealed

that the current PET/CT scanners number in Turkey jumped to 2.01 per 1 000 000 population and the estimated PET/CT frequency is nearly 7.66 scans per 1000 population. Better information is available on CT frequency than on PET/CT. The CT frequency in Turkey is 206.6 as compared to OCED average of 147.03 CT/ 1000 population/year [13].

The administered activity is highly dependent on the acquisition techniques and the sensitivity of the PET/CT scanner, however, the lowest possible dose must be used to yield the required image quality. At our site, the injected activity to each patient is routinely specified as 7.4 MBq/kg (0.2 mCi/kg) in SIEMENS and 3.7 MBq/kg (0.1 mCi/kg) in GE scanner. The average injected activity to our patients was found to be 421 MBq and the median value was 417 MBq. In contrast, the activity amounts used for the patients undergoing PET/CT via GE was only congruous with the current North American Consensus Guidelines for Pediatric Administered Radiopharmaceutical Activities which recommended 3.7–5.2 MBq/kg (0.10–0.14 mCi/kg) for a body ^{18}F -FDG PET/CT scan [14]. Moreover, the average activity of our population (421 MBq) was closer to the diagnostic reference levels (DRLs) in UK and Austria (400 MBq), while it was relatively higher than both Korea with DRL of 370 MBq in 2019 and Japan which has recently reported DRL of 240 MBq in 2020 [15, 16, 17]. In consideration of these factors, it is unlikely that in other countries in Europe or in OECD countries, the rate of occurrence of multiple imaging and doses may be lesser than ours.

These results indicate the need to analyse imaging appropriateness to know the extent to which imaging is in accordance with available guidelines. A recent study pertaining to CT imaging indicated that the large part of the imaging in cohort with high patient doses was in fact appropriate [18]. But that study was from a hospital which had clinical decision support (CDS) system in place for more than a decade which is not the case at our hospital or in our country and rather in most part of the Europe. In addition, the referenced study [18] also indicated that more than half of CT exams were unrelated to follow-up of a primary chronic disease. That goes against the common belief that patients undergo multiple imaging for follow-up of the chronic disease and it creates the need for analysing imaging appropriateness all the more at centers where CDS is not used. Another conclusion from the same study [18] was that imaging guidelines and appropriateness use criteria are not available for many conditions. Wherever available, they are for initial work-up and diagnosis and there is a lack of guidance on serial CT imaging. These conclusions hold all the more for PET/CT imaging as the available guidelines from professional societies for FDG-PET/CT [7, 14] are not detailed to cover a wide range of clinical conditions and indications for which recurrent imaging may be performed. Our analysis is just a snapshot, not comprehensive.

At present, all vendors provide CTIvol and DLP not only on the console display but the information is channelized through DICOM header and radiation dose structured report (RDSR) in the patient file in picture archiving and communication system (PACS) for permanent record in the patient file. The exposure factors are used by software to estimate E using chosen phantom [19]. Unfortunately, at the present moment there is no agreed methodology in place for estimating effective dose from radiopharmaceutical in view of differences in biokinetics and models involved [20]. Thus, modern dose management systems do not typically provide dose from radiopharmaceutical part just as they do for CT

part [20]. Despite limitations of E, it has not been replaced and in fact for multiple exams of a single patient covering different body parts, it remains the only dose quantity and as a result it has been used increasingly [21, 22]. ICRP in its recent report has clarified use of E that allows use of this dose quantity albeit with understanding for situations where there were doubts of its use [19, 22]. It is hoped that better information on patient-specific dose shall become available in the coming years.

Some limitations of the study are discussed. For example, in view of the non-availability of modern dose management systems that can automatically provide dose computations for a large number of patients, each patient's dose estimation was not possible in our study and average scan length and CTDIvol was employed and the interpatient variability was not considered. Also, patient-specific E estimation from internal emitters (^{18}F -FDG) requires carrying out subsequent scans over time intervals which was a further shortcoming in our retrospective study. However, the estimated mean E from ^{18}F -FDG PET/CT was well-correlated with the reported dose estimates in more dedicated studies [23–28].

Conclusion

It is clear that this study opens the door to many studies in future to deal with variety of issues pertaining to safety of patients who undergo a series of recurrent FDG-PET imaging. We have only been able to draw attention to high frequency of use of FDG-PET imaging

Declarations

Data Availability

The datasets generated during and/or analysed during the current study are available from the corresponding authors upon request.

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No funds, grants, or other support was received

Conflicts of interest/Competing interests

The authors have no conflicts of interest to declare that are relevant to the content of this article

Ethical Approval

This study was approved by the ethics committee of Cerrahpasa Medical School under decision No. 83045809-604.01.02-.

Consent to participate

Not applicable

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Figures

Figure 1

Frequency of the patients who underwent multiple 18F-FDG scans (2,3,4, and 5 times) in a year depicted for each year separately

Figure 2

Frequency of patients underwent a single and multiple 18F-FDG scans (1,2,3,4, and..23 times) over 11 years

Figure 3

Patients indications to 18F-FDG PET/CT scan