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ORIGINAL PAPER

Patients undergoing multiple ^{18}F-FDG PET/CT scans: frequency, clinical indications, and cumulative dose

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Abstract

Objective 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. The effective dose was estimated 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 a separate patient in different years). The maximum PET/CT scans in a year for any patient was five. 23,571 (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 a malignant disease, and 2.4% of patients with ≥ 2 ^{18} scans in a year had 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 largest ever study covering analysis of 11-years' data of ^{18}F-FDG PET/CT patients showed that a sizeable number of patients, largely with malignant disease (82%) undergo recurrent imaging during one year and non-ignorable fraction exceed 100 mSv in one year.

Keywords ^{18}F-FDG PET/CT doses · Cumulative effective dose · Multiple FDG scans · Recurrent imaging

1 Introduction

^{18}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 [1–3]. FDG is an analogous agent to vital glucose; therefore, the amount of FDG consumed or taken up by the cells expresses the respective metabolic status.

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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 local/regional/ national or international recommendations. 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 possible to adjust the exposure parameters according to the indications or the desirable clinical needs. In common practice, a low-dose CT protocol is a well-established method for attenuation correction and anatomic localization. However, the exposure factors are higher when a diagnostic CT image with greater details is required either with contrast enhancement or without contrast. In any case, the radiation dose from PET/CT scans has been a matter of concern [8, 9].

A review of the literature indicates a paucity of information on the assessment of the frequency of PET/CT imaging for patients, clinical indications involved in recurrent imaging, and cumulative dose, except for one recent publication in 2022 from a single large center in the USA based on 2-years of data collection [10]. Our study includes data analysis for 11 years which has not been done so far by any study. In this large study, we have assessed how often a patient undergoes ^{18}F-FDG PET/CT exams, the age distribution of patients who undergo multiple exams, their diagnoses, and the cumulative radiation doses received.

2 Methods

Medical records of patients subjected to ^{18}F-FDG PET/CT scan were retrospectively analyzed for nearly 11 years from 04 to 2010 to 04 Nov 2020. This retrospective study was approved by the ethical committee. 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. The flow diagram in Fig. 1 below describes the process.

PET/CT scans were routinely acquired with cranially extended torso imaging protocol from top of head to midthigh 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. Table 1 summarizes the specifications of PET/CT systems and imaging parameters. Since 2014, the 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 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 IDs 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 ^{18}F-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 ^{18} F-FDG was estimated using the dose conversion coefficient of 0.019 mSv/MBq as provided by ICRP Publication 128 [11].

For estimation of E from CT scans, the region-specific conversion coefficients (CFs) from dose length product (DLP) to E were summarized by Deak and co-authors [12]. The CF at 120 kVp was reported to be 0.0019, 0.0051,

Fig. 1 The study flow diagram

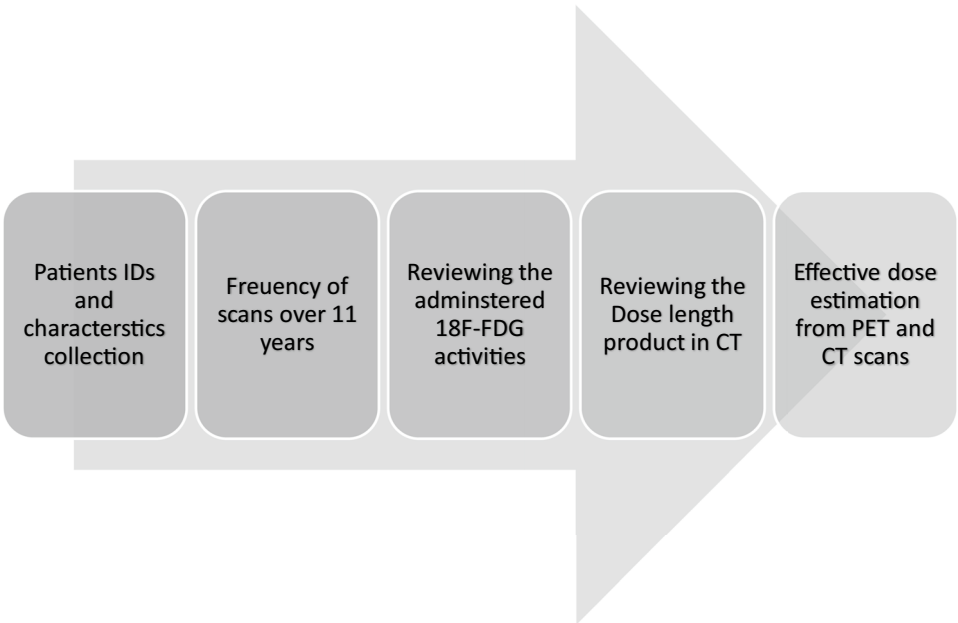


Table 1 Specifications of two PET/CT scanners used in this study

GE discovery 710	Siemens biograph 6
4.2 × 6.2 × 30 mm^3 LYSO (Lutetium yttrium oxyorthosilicate) crystals	6.4 × 6.4 × 25 mm^3 LSO (Lutetium oxyorthosilicate) crystals
16 slices CT scanner (helical mode)	6 slices rotating CT scanner
120 kVp, tube current modulation typically with 35–215 mA	130 kVp/ ≈ 35–290 mA
0.7 s rotation time, 18.8 mm table feed per rotation	4 mm slice thickness
16 × 1.25 mm collimation width, and 0.938 pitch limit	0.921 s rotation time

0.0145, 0.0153, and 0.0129 for the 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 and 120 kVp was used for the GE Discovery scanner, the average of the conversion coefficients for chest, abdomen, and pelvis was 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 (the scan length ranged from 80 to 140 cm when the total body is involved).

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

$$\text{Total E} = \text{E from PET part} + \text{E from CT part}$$

$$\text{Total E} = [n \times A(\text{MBq}) \times 0.019(\text{mGy/MBq})] + [n \times CF \times DLP]$$

E: effective dose, n: number of scans, A: administered ^{18} F-FDG activity, CF: conversion factor, DLP: dose linear product (mGy.cm^2).

3 Results

During the observation period of ≈ 11 years, the total number of 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 in all population was found to be 421 MBq and the median value was 417 MBq.

3.1 Frequency assessment of patients with recurrent scans

Table 2 indicates that 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). A total of 5430 patients (16.6%) 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. No patient was scanned with ^{18} F-FDG more than 5 times in a year.

Figure 2 depicts visually the year-wise distribution of the number of patients who received 2,3,4 or 5 ^{18}F-FDG scans in any individual year.

When the patients with 2–5 scans in a year were pooled together as shown in Tables 3 and 2442 (7.4%) out of 7898 patients were found duplicated (repeatedly scanned ≥ 2 times in multiple years) and the absolute patients' number decreased to 5456 (16.7%) by counting the unique IDs.

When consolidated over the entire period of about 11 years, the total number of scans ranged between 1 and 23 for the patients population as illustrated in Fig. 3. 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 did not get detected when we used the criteria of 2 or more scans in a single year. In further elaboration, Table 4 comprehensively demonstrates all the patients who were 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, 13,045 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

Table 2 Gender identity of the patients who underwent ≥ 2 ^{18}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%)
Sum	4897 (15.0%)	3001 (9.2%)	7898 (24.2%)

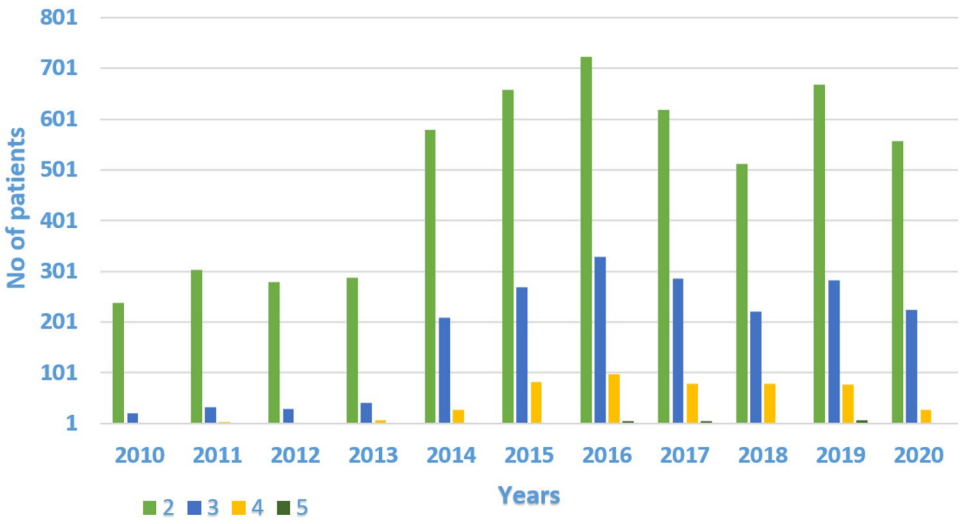


Fig. 2 Frequency of the patients who underwent multiple ^{18}F-FDG scans (2, 3, 4, and 5 times) in a year depicted for each year separately

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.

Figure 3 presents data of 11 years pooled together. It was apparent 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.

3.2 Main clinical indications of patients with multiple scans

The clinical indication for ^{18}F-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 Fig. 4. 2.4% of the patients with ≥2 ^{18}F-FDG PET/CT scans in a year were with non-malignant indications, and likewise 3% of those scanned ≥2 times over 11 years.

Table 3 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%)**

3.3 Dose assessments

The CTIvol was obtained from the dose reports obtained at the end of the scan for these patients. The mean CTIvol (32 cm phantom) in GE was 12.4 mGy, while it was 6.3 mGy in Siemens for chest to femur region in scan. The mean 16-cm CTIvol for Siemens was for brain PET/CT scans was 13.2 mGy, and 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 for the head and neck region.

The average effective dose to an individual patient following a single ^{18}F-FDG PET/CT scan was estimated as 25.0 mSv from GE and 19.2 mSv from Siemens, which leads further to a dose with a higher number of scans, as shown in Fig. 5. Overall, 446 patients (1.4%) received a total effective dose of 100 mSv or more in one year from multiple ^{18}F-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 ^{18}F-FDG

Table 4 Total number of patients with 2–23 ^{18}F-FDG PET/CT scans over 11 years filtered by scans in a year involving unique and duplicated subjects

Scans in a year (sc-y)	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	13,045	6521	6524
2	5430	4450	980
3	1952	1529	423
4	488	435	53
5	28	28	0

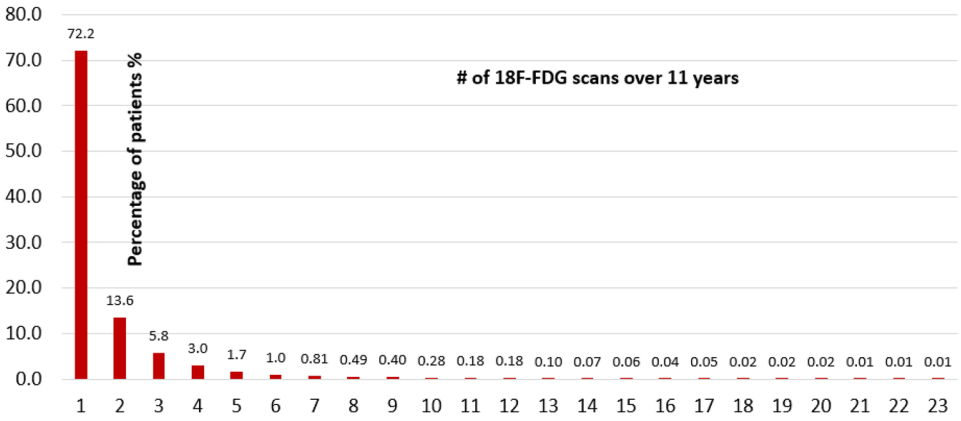


Fig. 3 Frequency of patients who underwent single and multiple ^{18}F-FDG scans (1,2,3,4, and 23 times) over 11 years

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.

4 Discussion

The important findings of this largest ever 11-year study covering 55,424 ^{18}FDG-PET/CT exams in 32,658 patients for assessing the frequency of patients with multiple exams include: 24.2% patients scanned 2–5 times in a year, 16.7% of them being unique patients (not counted as a separate patient in multiple years); the maximum number of PET/CT scans in a year of 5; 82% of the patient cohort with malignant disease; 2.4% of the patients with ≥ 2 ^{18}F-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 ^{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 38 to 575 mSv (median: 271 mSv). It must be noted that 100 mSv is neither a dose limit nor threshold for radiation effect, but a number of organizations including UNSCEAR [13] have mentioned a low dose as dose below 100 mSv and it has been used in recent years as a level in many recent studies to draw attention to high doses [10, 14, 15].

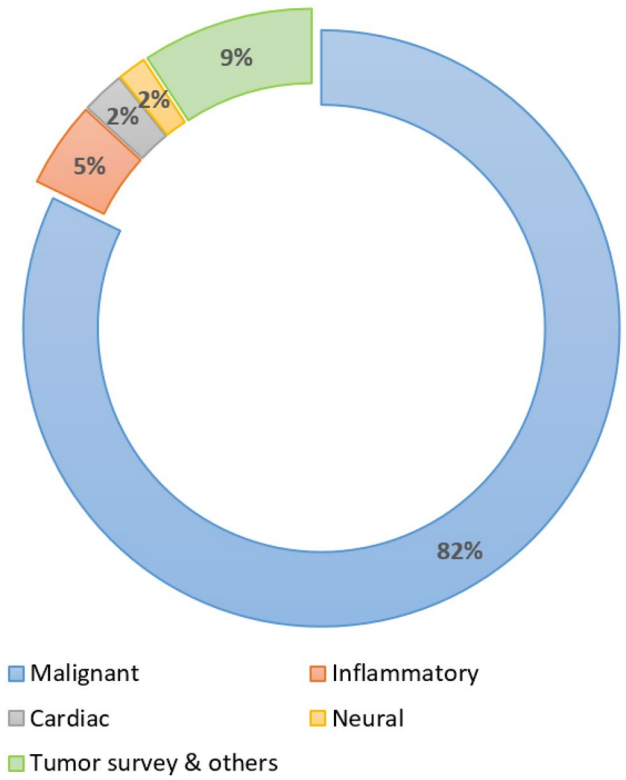


Fig. 4 Patients indications to ^{18}F-FDG PET/CT scan

This comprehensive study is the largest study, 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 population in 2019 according to OECD publication [16]. 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 [16]. 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 the OCED average of 147.03 CT/ 1000 population/year [17].

It is well known that the administered activity is highly dependent on the acquisition techniques and the sensitivity of the PET/CT scanner. At our site, the injected activity to each patient is routinely specified as 7.4 MBq/kg (0.2 mCi/kg) for imaging on the Siemens system and 3.7 MBq/kg (0.1 mCi/kg) for the GE scanner. The variation in the injected

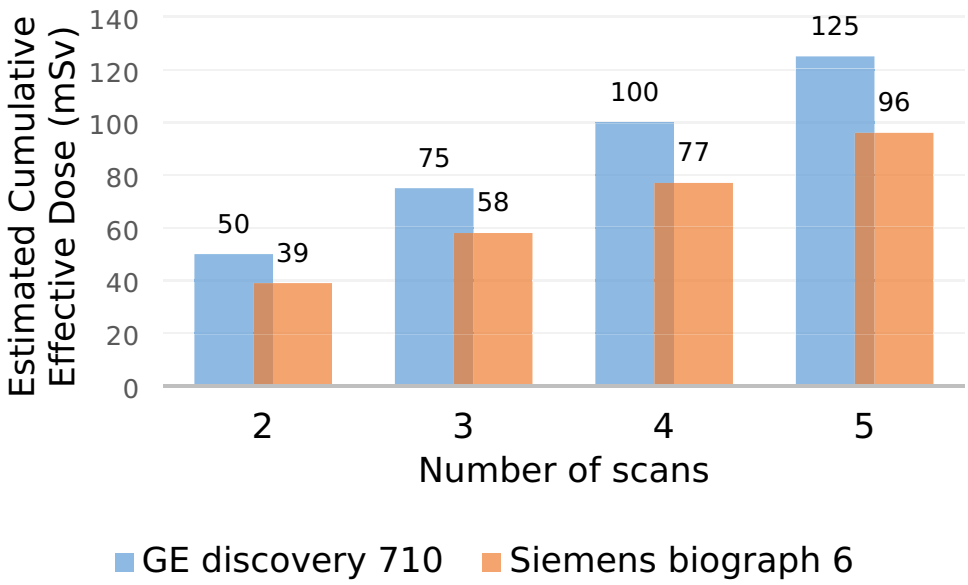


Fig. 5 The estimated cumulative effective dose (CED) of individual patients from ^{18}F-FDG PET/CT scans

activity relates to the difference in the detection efficiency between the earlier used Siemens PET/CT scanner and the more recently installed GE with spiral CT dataset. The average injected activity into 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 were only congruous with the current North American Consensus Guidelines for Paediatric 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 [18]. 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 a DRL of 370 MBq in 2019 and Japan which has recently reported DRL of 240 MBq in 2020 [19–21]. In consideration of these factors, it is unlikely that in other countries in Europe or in OECD countries, the doses may be lesser than ours. The frequency of imaging may likely be more in many developed countries.

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 a large part of the imaging in patient cohort with high patient doses was in fact appropriate [22]. But that study was from a hospital in the USA 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 parts of Europe. In addition, the referenced study [22] also indicated that more than half of CT exams were unrelated to the 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 [22] was that imaging guidelines and appropriateness use criteria are not available for CT imaging for many conditions from the American College of Radiology (ACR). 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, 18] 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 as the primary objective of our study was to identify the problem and assess its magnitude. We anticipate it will create interest among many investigators to further analyse causes and develop solutions. Concurrently, a study from a major hospital in the USA just published shows that a sizeable number of patients undergo ≥ 2 ^{18} exams with one out of every 8 patients receiving a cumulative dose ≥ 100 mSv and that includes patients with long life expectancy [10]. Further, our attention has been drawn to a recent joint statement of AAPM/ACR/HPS [23] cautioning against use of doses from a patient's prior imaging exams for the purposes of medical decision-making for the next exam. Neither are we aware of publications where there has been misuse of doses from previous imaging exams or cumulative doses, nor did the above joint statement cite any reference to indicate evidence of such misuse. On the contrary, there is evidence of appropriate use and enhancement in justification and optimization achieved as a result of tracking of procedures and doses [24]. Further, a recent special focus issue of Br J Radiology contained a series of publications on tracking doses, and the editorial [25] stated: "Despite

evidence lacking in reported literature of potential misuse of cumulative doses to refuse a needed examination, there remains the fear of misuse of cumulative dose. Future steps must be evidence-based rather than driven by repercussions. Training needs to be strengthened to include a better understanding of contemporary and new issues pertaining to cumulative dose to avoid misuse and misunderstanding". Moreover, there have been two position statements issued by the International Atomic Energy Agency in cooperation with several professional organizations and international bodies such as WHO encouraging tracking of patient exposure [26, 27]. Tracking of doses has led to the identification and assessment of the problem, making us realise that we are in an unprecedented era [25, 28, 29]. Unfortunately, the clinicians who refer patients for imaging have hardly been involved in such efforts, but when involved, they see a value in knowing doses from previous exams [30].

At present, all vendors provide CTIvol and DLP not only on the console display, but the information is channelized through the 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 [31]. Unfortunately, at the present moment, there is no agreed methodology in place for estimating effective dose from radiopharmaceuticals in view of differences in bio-kinetics and models involved [32]. Thus, modern dose management systems do not typically provide doses from radiopharmaceutical parts just as they do for CT part [32]. Despite the 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 [33, 34]. ICRP in its recent report has clarified the use of E that allows use of this dose quantity albeit with understanding for situations where there were doubts of its use [31, 34]. It is hoped that better information on patient-specific dose shall become available in the coming years. Moreover, there are indications that ICRP may change the dose co-efficient for ^{18} F-FDG which will have an impact on dose estimates.

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 were 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 [35–40]. Future studies may also include further analysis of clinical data presented in Fig. 3 to have a better understanding of the clinical indications leading to high cumulative doses. In such a large study done with manual data collection, it was not possible to assess the percentage of studies that had CT only for attenuation correction. Future studies may need to do that to have a better data analysis.

5 Conclusion

It is clear that this largest-ever 11-year study opens the door to many studies in the future to deal with a variety of issues pertaining to the safety of patients who undergo a series of recurrent FDG-PET imaging. Our work involved identifying and assessing the magnitude of multiple PET/CT imaging in an individual patient, the doses involved, and a rough and broad indication of clinical conditions associated with these patients. We found that typically 1 out of every four patients was scanned 2 to 5 times a year. Nearly 80% of patients had the malignant disease. The cumulative effective dose of 9087 (27.8%) patients who underwent 2 to 23 ^{18}F-FDG PET/CT scans over 11 years ranged from 38 to 575 mSv (median: 271 mSv). Among them, 2415 patients (27%) had CED above 100 mSv during 11 years. The study creates the need for analysing imaging appropriateness where the clinical disease support system is not used.

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

Declarations

Ethical approval This study was approved by the ethics committee xxxxx under decision No. 83045809-604.01.02-.

Consent to participate Not applicable.

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

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