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Quantitative FDG PET/CT in the Community: Experience from Interpretation of Outside Oncologic PET/CT Exams in Referred Cancer Patients

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Abstract

Purpose—Tertiary care institutions often deal with patients who have had a baseline PET/CT scan performed elsewhere. Little data exists regarding the quality of these PET/CT scans and whether they are fully suitable for qualitative or quantitative interpretation. We evaluated outside PET/CT scans from cancer patients referred to our institution and compared them to PET/CT scans acquired locally.

Methods—This HIPAA-compliant retrospective study was approved by our institutional review board. Informed consent requirements were waived. 170 recent whole-body outside PET/CT exams from many sites were digitally imported into our radiology imaging system and reviewed for key quality metrics including time from injection until imaging, availability of patient height and weight information, serum glucose level, and FDG dose. The standardized uptake value (SUV) and standardized uptake value based on lean body mass (SUL) in the liver were measured whenever possible. These were compared to 170 internal studies performed at our center during the same period.

Results—Missing data were common in outside scans with height in 62%, weight 35%, uptake time 25%, FDG dose 28%, and glucose levels in 64% of cases. In quantitatively evaluable cases, mean liver SUL, SUV, FDG dose, and uptake time were much more variable in outside than in internal studies.

Conclusion—Approximately one third of the outside PET/CT studies submitted digitally for analysis lacked key information required to secure any quantitative imaging data. Only about a third of these studies had all necessary information available for accurate SUL determination and had acceptable quality that was comparable to locally acquired scans. This suggests that many of PET studies performed in the community cannot be relied upon to provide quantitative image data that can be applied in a different center. Greater standardization of oncologic PET/CT studies among different centers must still be pursued.

Keywords

PET/CT; Quantitative PET; SUV; FDG; standardization

Introduction

Positron emission tomography (PET) using [^{18}F] fluoro-2-deoxy-D-glucose (FDG) is recognized as an important clinical tool, particularly in oncology. FDG PET is now routinely used in the detection, staging, evaluation of treatment response and prognosis in various cancers (1, 2).

Although visual inspection of FDG PET images remains very important for diagnosis and response assessment, it has been shown that semiquantitative analysis with standardized uptake values (SUV) allows for a more objective assessment of lesion characterization, prognostic stratification, and monitoring treatment response (3, 4). Treatment response is generally evaluated based on the relative change of SUV during treatment. At the same time, comparison of SUV results obtained from different centers is hampered by the large variability in the methodology of acquisition, image reconstruction, and data analysis procedures applied.

Tertiary care institutions often care for patients who have had a baseline PET/CT scan performed at another center. Reimbursement rules frequently will not allow for performance of a new baseline study after the patient has had a PET/CT exam at another center. It is often necessary that subsequent PET/CT scans obtained at the tertiary center have to be compared to the outside baseline scan for therapy assessment and restaging. Little data exists regarding the quality of PET/CT scans obtained in the community and whether or not they are suitable for quantitative interpretation.

The need for standardization was addressed more than a decade ago by Young et al. (5). The authors discussed various methods for quantification of FDG-PET studies, such as visual inspection, use of SUV, or full kinetic analysis. Factors affecting FDG uptake were described, and a set of recommendations was presented. Shankar et al. (6) later published the consensus recommendations for FDG PET studies as an indication of the therapeutic response in patients in National Cancer Institute (NCI) Trials. The guidelines focus on patient preparation, image acquisition, image reconstruction, quantitative and semiquantitative image analysis, quality assurance, reproducibility and other factors in FDG PET studies before and after a therapeutic intervention. More guidelines are being developed as the use of PET/CT has become more widespread (7).

More quantitative approaches to assessment of response to treatment with PET such as PERCIST 1.0 have been proposed (8). Graham et al. (9) published an article on the variations in PET/CT methodology for oncologic imaging at U.S. academic Medical Centers. They concluded that there is considerable variability in the way PET/CT scans are performed at academic institutions that are part of the IRAT (Imaging Response Assessment Teams) network funded by the National Cancer Institute (NCI) as supplemental grants to existing NCI Cancer Centers. This variability is likely to make it difficult to quantitatively compare studies performed at different centers.

In the current study, we compared PET/CT scans from our own center to scans from outside centers for cancer patients referred to our institution to establish their suitability for quantitation.

Materials and Methods

Institutional review board approval was obtained for this Health Insurance Portability and Accountability Act–compliant retrospective review of PET/CT images; informed consent requirements were waived. A sequential total of 170 recently obtained outside PET/CT exams from 99 different performance sites for cancer patients, referred to our institution for further workup and treatment, were included as the “outside study group”. Only whole-body scans were included. A similar sequential 170 cohort of studies performed around the same time at our own PET center were included as the “internal study group”.

The outside studies available in a digital format were transferred to a GE Advantage Workstation for reading. We reviewed key quality metrics including FDG dose injected, time from injection until imaging, and availability of patient height and weight information. This information is usually extracted from the header file available in the CD brought by the referred patient and uploaded with the scan. These patients were not seen in person in our PET/CT center. Average SUV and SUV based on lean body mass (SUL) in the liver were determined whenever possible.

The mean SUV of the liver was measured by placing a spherical region of interest (ROI) with a 3-cm diameter in the posterior right lobe of the liver in a lesion-free area. The standardized uptake value is then determined using the definition,

$$SUV = \frac{\text{Radiocativity concentration in tissue (MBq/ml)}}{\text{Injected dose (MBq) / patient's body weight (g)}}$$

This parameter is unitless (assuming tissue density of 1 g/ml) and computable only when the injected dose and the weight are known.

Standardized uptake value based on lean body mass (SUL) is determined using lean body weight instead of the patient's body weight in the above expression. This requires that information about the height of the patient be available.

The parameters necessary for the computation of SUV or SUL was extracted either from the header file of the PET/CT scan or from the clinical report. This latter is often brought by the patient in printed form and scanned locally as an electronic document linked with the images. Sometimes this report is saved electronically on the CD containing the PET/CT images and sent with the referred patient.

Statistical comparisons between the group of the outside scan and the local group were performed by computing mean, standard deviation, and coefficient of variation for all parameters. An F test for comparison of variances was applied. Significance was set at $P=0.05$. Statistical analysis was performed using SPSS (version 20; SPSS Inc.)

Results

For the outside PET/CT studies, the average patient age was 57.7 ± 14.9 years (mean $\pm$ STD), with 91 females and 79 males. The mean age for the internal study group was 54.2 ± 16.5 years, with 88 females and 82 males.

The 170 outside PET/CT exams included in this study were from 99 different sites. 13 of these sites were academic and 86 community centers. Community centers here are PET/CT centers that are not affiliated with a University or an academic center.

PET parameters

The value for the weight of the patient was available for 110 out of the 170 outside scans examined (65%), meaning that more than one third of the outside studies lacked information about weight, as it was not recorded in the header file or available in the outside report.

Height was recorded and provided for 64 studies (38%). A little less than two thirds of the outside studies did not provide the height of the patient, information needed for the determination of SUL.

The information about the FDG dose injected was provided for 123 studies of the 170 outside studies examined (72%). The uptake time from injection to scan was provided for 127 studies (75%). Plasma glucose at the time of injection was provided for 61 patients (36%).

The lack of availability of the necessary parameters made impossible the computation of the average liver and the average liver SUV for an additional 52 studies (31%). This information is summarized in table 1 and figure 1.

For the outside studies, plasma glucose at the time of injection, when available, ranged from 68 to 177 mg/dL, with an average of 101.5 ± 18.6 mg/dL. The time from injection to scan ranged from 21 to 143 minutes, with an average of 69.5 ± 25.1 minutes. The FDG dose injected averaged 503 ± 170 MBq (13.6 ± 4.6 mCi), ranging from 85.1 to 888.0 MBq (2.3 to 24.0 mCi). The average weight was 74.9 ± 24.6 Kg (information available for 65 % of patients). This translated into an FDG dose per Kg of 7.3 ± 2.5 MBq/Kg (0.20 ± 0.07 mCi/Kg) (range: 3.0 – 13.3 MBq/Kg; 0.08-0.36 mCi/Kg). Average height was 165.9 ± 23.4 cm (information available for 38 %).

The average liver SUL for outside PET/CT studies was computable for only 63 scans (37% of the total). It averaged 1.6 ± 0.4 , and ranged from 0.4 to 2.7. The average liver SUV ranged from 0.6 to 5.8 and averaged 2.2 ± 0.6 . It was possible to determine the SUV for 115 out of the 170 outside scans (67.6%).

By comparison, 170 in-house studies performed around the same time at our center had a mean plasma glucose of 99.7 ± 19.4 mg/dL (range from 68 to 203), an injection to scan time of 61.5 ± 9.1 min (range 46 to 102), FDG dose: 569.8 ± 159.1 MBq (15.4 ± 4.3 mCi) and range: 103.6 to 958.3 MBq (2.8 to 25.9 mCi). The average weight was 75.2 ± 20.9 Kg FDG dose per Kg: 7.6 ± 1.0 MBq/Kg (0.21 ± 0.03 mCi/Kg) and range 4.4 – 11.3 MBq/Kg.

(0.12-0.30 mCi/Kg). Average height was 168.5 ± 12.0 cm. The average liver SUL was 1.5 ± 0.3 (range 0.6 to 2.2), and the average liver SUV was 2.1 ± 0.4 (range 0.8 to 3.1).

There was significantly larger variation in the injection-to-scan time and the FDG dose per Kg injected for outside vs. local studies ($p < 0.001$). There was no statistically significant difference in the COV values for the FDG dose, liver mean SUV or SUL.

Table 2 provides a summary of the quantitative comparison between outside PET/CT scans and studies performed locally at our center.

CT component

For the CT component of the outside PET/CT studies, 5 scans (3% of total) contained PET images only, 19 scans (11%) did not have usable CT parameter data (CD with proprietary software or only fused images available), 132 scans (78%) had CT done without an IV contrast injection, 14 scans (8%) were done with IV contrast. See figure 2. In terms of current modulation, 80 CT scans (47% of total) were acquired with a Xray tube using current-modulation techniques. The remaining 90 scans (53%) used a fixed X-ray current. The X-ray current mean was 116 ± 60.6 mA (range: 30 - 360 mA). By contrast, the CT component of in-house PET/CT scans used for localization and attenuation correction purposes was performed with no IV contrast. The X-ray voltage source was fixed at 120 kVp for whole body scans. All CT scans were performed using current-modulation techniques with a maximum set at 200 mA for adults. For pediatric patients, a weight-based fixed current was used. Example: for weights less than 7.5 kg, a fixed current with 20 mA was used. A fixed current with 60 mA was used for 40 – 55 kg weights.

Discussion

Quantitation is increasingly important in PET/CT interpretation. Decisions about staging, assessment of response to therapy and prognostic evaluation relies more and more on comparison of standardized uptake values. However, many of the outside PET/CT studies from patients referred to our center lacked one or more of the key elements necessary for minimal quantitative evaluation that would make comparison with future studies possible. As computation of SUV and SUL requires information about weight, height, dose of FDG injected, and injection-to-scan times, semi-quantitation using these standard uptake values was not possible as information about one or more of these parameters was not provided either in the header file or the report accompanying the scan.

Only about one third of the outside scans had enough information necessary for the computation of SUL. SUV was possible to determine for about an additional one third. The only reason it was not possible to obtain the SUL was that the height of the patient was not measured or recorded in the header file. This information was usually not available on the outside report either. About one third of the outside PET/CT scans were not suitable for any kind of quantitative or semi-quantitative evaluation. While SUV or SUL can be calculated, we do not know precise calibration methods for the outside scanner and dose calibrator. Thus absolute quantitation can be inaccurate.

The lack of minimal meaningful quantitation coupled with a wide variation in techniques of acquisition and patient preparation means that it is quite difficult to use the scan acquired in the community as a baseline scan for future comparison with scans acquired locally. If the technique used for acquisition of the outside study varies markedly from the local one, the baseline scan will often need to be repeated. Unfortunately, the payor rules of many insurance companies will not allow performance of a new baseline study after the patient has had a PET/CT exam at another center. When the PET/CT studies acquired in the community have enough information to enable the computation of the SUV or the SUL, it is a little encouraging that the values obtained are generally comparable to the ones performed locally as judged by the mean values and the spread of the mean liver SUL (1.6 ± 0.4 for outside studies vs. 1.5 ± 0.3 for local studies). This also holds for liver SUV, although there is slightly more spread in the outside studies.

There was significantly larger variation in the injection-to-scan time and the FDG dose per Kg injected for outside vs. local studies ($p < 0.001$), table 2. At our institution, patients are administered an FDG dose proportional to their weight, 8.1 MBq (2.2 mCi) of ^{18}F -FDG per kilogram up to about 925 MBq (25 mCi) and incubated for a period of 60 min.

The study by Pacquet et al. (10) evaluated the intra-patient test-retest variability of SUV, and some derived parameters like SUL, in liver and other normal tissues and concluded that the SUVs measured in normal liver and mediastinum in cancer-free patients are stable over interval time between PET/CT studies. The authors found a population variation of liver SUV and SUL between the two studies of 11.0% and 10.8%, respectively. The values of mean liver SUV and SUL found by the authors are 2.02 ± 0.39 and 1.49 ± 0.25 on the patients' first scans, respectively. These are consistent with our local values. A more recent paper by Laffron et al. (11) found normal human liver SUV was stable over uptake time in FDG PET imaging if the time delay between tracer injection and PET acquisition is in the range of 50–110 min, and was within 5% of its peak value during this interval. The larger variation in the injection-to-scan time in the outside studies is therefore concerning.

The variability of the FDG dose in the outside studies is also concerning as it has a direct bearing on the radiation dose to the patient. As expected from the patient population included, mainly cancer patients, there was no significant variation in the plasma glucose, at least for the studies where this information was available.

Certainly, there is ample room for improvement since technical parameters associated with the acquisition of PET/CT scans, such as the dose of FDG injected and the injection to scan time, fall within NCI recommended guidelines.

The CT component of PET/CT scans from the community varied greatly in the X-ray tube current. Less than half of the outside scans used the technology of current-modulation, shown to reduce the radiation dose to the patient (12–15). Most of the scans were performed without IV contrast, with less than 10% done with IV contrast. Reductions in dose from CT as part of PET/CT appear quite feasible and practice patterns are quite heterogeneous. In an era when radiation dose related to CT scans has become a public health concern, every effort

should be invested to reduce the radiation dose to patients from imaging scans while preserving diagnostic accuracy.

These observations suggest that a large fraction of PET studies performed in the community cannot be relied upon to provide meaningful quantitative imaging data that can be applied in a different center. Opportunities for greater standardization among centers abound. The technique would significantly benefit from standardization, particularly as we try to identify new indications for reimbursement, and for meaningful and reproducible quantitative imaging to assess response to therapy, especially for patients with a baseline scan performed at a different center.

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Outside PET/CT studies

Figure 1. Adequacy of outside PET/CT studies for semi-quantitative analysis

Figure 2. General characteristics of the CT component of outside PET/CT studies

Table 1

Summary of available information needed for quantitation assessment of outside PET/CT studies. This information is either recorded in the header file or written in the outside report accompanying the scan, if available. While SUV or SUL can be calculated, we do not know precise calibration methods for scanner and injected dose. Thus absolute quantitation can be inaccurate.

Outside Studies		
	Number	Percentage of total
Total	170	100%
Weight	110	65%
Height	64	38%
FDG dose	123	72%
Injection-to-scan time	127	75%
Plasma glucose	61	36 %
Adequate for SUL and SUV	63	37%
Adequate for SUV only	105	68%
Not adequate for any quantitation	55	32%

Summary comparison between outside PET/CT scans and studies performed locally

Table 2

	FDG dose (MBq)	FDG dose per Kg (MBq/Kg)	Plasma glucose (mg/dL)	Injection-to-scan time (min)	Liver Mean SUV	Liver mean SUL
Outside Studies	503.0 ± 170.0	7.3 ± 2.5	101.5 ± 18.6	69.5 ± 25.1	2.2 ± 0.6	1.6 ± 0.4
	Range: 85.1-888.0	Range: 3.0-13.3	Range: 68-177	Range: 21-143	Range: 0.6-5.8	Range: 0.4-2.7
N = 170	COV = 0.34	COV = 0.34	COV = 0.18	COV = 0.36	COV = 0.27	COV = 0.25
	N = 123	N = 110	N = 61	N = 127	N = 115	N = 63
Local studies	569.8 ± 159.1	7.6 ± 1.0	99.7 ± 19.4	61.5 ± 9.1	2.1 ± 0.4	1.5 ± 0.3
	Range: 103.6-958.3	Range: 4.4 – 11.3	Range: 68-203	Range: 46-102	Range: 0.8-3.1	Range: 0.6-2.2
N = 170	COV = 0.28	COV = 0.13	COV = 0.19	COV = 0.15	COV = 0.19	COV = 0.20
	N = 170	N = 170	N = 170	N = 170	N = 170	N = 170
Variance ratio	1.1	6.1	1.1	7.5	2.1	2.0
	NS	P < 0.001	NS	P < 0.001	NS	NS

COV: coefficient of variance, NS: not statistically significant