Determining the Optimal Dose of 18F-FDG for Hodgkin lymphoma Imaging on PET/CT Camera with BGO Crystals

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Abstract

**Purpose:** We aimed to find the minimum feasible dose of fluorodeoxyglucose (18F-FDG) in positron emission tomography/computed tomography (PET/CT) of Hodgkin lymphoma patients performed on a camera with bismuth germanate (BGO) crystals.

**Methods:** Ninety-one 18F-FDG PET/CT scans with decreasing time per bed position (2 min, 1.5 min, 1 min, 50 sec, 40 sec, 30 sec and 20 sec) were assessed to evaluate image quality. Mean administered dose was 3.0±0.1 MBq/kg and mean uptake time was 54.0±8.7 min. The series quality was subjectively marked in 1-10 scale and then ranked 1-7 based on the mean mark. Interobserver rank correlation and intraclass correlation within each series were calculated. Phantom studies were also performed to determine if reduced acquisition time can be directly translated into a reduced dose.

**Results:** We show the longer the time of acquisition the higher the mark and rank. The interobserver agreement in ranking was 100% with kappa coefficient of 1.00 (95% CI [0.83-1.0]). The general intraclass correlation coefficient was 0.945 (95% CI [0.936-0.952]). Only the series with 2 min and 1.5 min acquisition time were appropriate for assessment (mean mark \(\geq 7\)). In phantom studies there was a linear correlation between time per bed, administered activity and number of total prompts detected by a scanner. Hence, reduction of acquisition time of 25% (from 2 min to 1.5 min) could be directly translated into a 25% dose reduction (from 3.0 to 2.25 MBq/kg).

**Conclusions:** In patients with HL, 18F-FDG dose can be reduced by up to 25% when using a BGO crystal camera, without substantial impact on image quality.

Introduction

The dual-modality positron emission tomography/computed tomography (PET/CT) has recently become a primary imaging method for a wide range of oncologic, cardiologic and neurologic diseases. It is used at various stages of the treatment process spanning from diagnosis, primary staging to treatment response assessment.

Despite its many advantages, PET/CT is a diagnostic method associated with radiation exposure seems and that may rise concern. Indeed, in a PET/CT examination the patients receives radiation dose from the radiotracer and from the CT. The effective dose of the 18F-2-fluoro-2-deoxy-D-glucose (18F-FDG) PET/CT may reach up to 30 mSv, depending on: the CT protocol (high-dose diagnostic CT vs low-dose CT for anatomic localisation); the radiotracer dose (the effective dose of 18F-FDG is 0.019 mSv/MBq); the anatomical region; and the number of body parts imaged [1, 2].

According to the guidelines–based on phantom experiments, theoretical estimations and retrospective studies on heterogenous populations–the administered activity of 18F-FDG should be 3.5-7 MBq/kg [3–8]. Currently, however, doses smaller than 4.0 MBq/kg are usually injected. In order to comply with the ALARA principle, which states that the patient should receive the dose As Low As Reasonably Achievable, PET/CT protocols are constantly optimised in order to further reduce the effective dose without compromising the image quality. In order to reduce the CT dose we may: decrease the tube voltage, tube current or the exposure time, and minimise the Z-axis coverage. In the PET protocol we may: use 3D acquisition mode or time-of-flight reconstruction, apply novel reconstruction algorithms such as Bayesian penalised likelihood (BPL), increase acquisition time per bed and, finally, reduce the injected dose [3, 5, 9, 10].

The aim of the study was to determine the minimum feasible 18F-FDG dose that would not compromise the quality of images in patients with Hodgkin lymphoma obtained from a PET/CT scanner with bismuth germanium oxide (BGO) detectors.

Materials And Methods

Patients

We retrospectively evaluated 18F-FDG PET/CT scans of patients with Hodgkin lymphoma (HL) referred to the Dolnośląskie Affidea PET/CT Centre for disease staging or response assessment between January 2017 and October 2018. Some of the patients had more than one scan included in the study – 1 patient had 5 scans included, 2 patients 4 scans, 13 patients 3 scans, 21 patients 2 scans and the remaining 14 patients had 1 scan each. Patient and PET/CT scan characteristics are summarised in Table 1.
Table 1

| CHARACTERISTIC            | VALUE                                                                 |
|---------------------------|----------------------------------------------------------------------|
| Number of PET/CT scans    | 91                                                                  |
| Number of patients        | 50                                                                  |
| Gender                    | 33 (66%) women, 17 (34%) men                                        |
| Age                       | mean ± SD 38.7 ± 16.5 years median (range) 34.0 (12.0–85.0) years   |
| Weight                    | mean ± SD 71.0 ± 13.5 kg median (range) 69.0 (37.0–101.0) kg          |
| BMI                       | mean ± SD 24.8 ± 4.2 median (range) 24.3 (14.8–35.4)                 |
| Administered activity     | mean ± SD 211.3 ± 40.3 MBq median (range) 208.3 (110.7–318.1) MBq     |
| Administered activity per kg | mean ± SD 3.0 ± 0.1 MBq/kg median (range) 3.0 (2.7–3.3) MBq/kg       |
| Uptake time               | mean ± SD 54.0 ± 8.7 min median (range) 52.0 (45.0–77.0) min          |

BMI – body mass index, SD – standard deviation, MBq – megabecquerels

Imaging Protocol

PET/CT imaging was performed using a 5-ring PET/CT system Discovery IQ with BGO crystals (GE Healthcare, Chicago, Illinois, US). A scout view and a non-contrast-enhanced low-dose helical 16-slice CT scan was performed for attenuation correction of the PET emission data and for anatomic localization.

The CT scan was acquired with a tube voltage of 100–140 kV. The X-ray tube rotation time was 0.6 s. The CT reconstructions were performed with a standard kernel with a slice thickness of 1.25 mm.

Immediately after CT scanning a whole-body three-dimensional PET was acquired. The scan range was from the top of the head to mid-thighs. For each bed position (24% overlap) a 2 min acquisition time was used. The images were then reconstructed with a stepwise reduction of time per bed (1.5 min, 1 min, 50 sec, 40 sec, 30 sec and 20 sec). The emission data was corrected for geometrical response and detector efficiency (normalization) as well as for system dead time, random coincidences, scatter and attenuation. Attenuation corrected images were reconstructed with Bayesian Penalised Likelihood (Q.Clear) algorithm. The matrix size was 256 × 256. The resolution recovery algorithm (GE SharpIR) was used. Q.Clear images were reconstructed with beta values of 350, no post filtering.

Image Analysis

PET/CT images were analysed with GE Healthcare Advantage Workstation (Chicago, Illinois, United States) independently by three experienced nuclear medicine physicians. The assessment was blinded - the time frame series were renamed by the supervising physicist before the evaluation. Each reviewer had seven series per scan—presented in a random order—to assess: one standard series with a 2 min acquisition time (1) and six series with reduced acquisition time (2) 1.5 min, (3) 1 min, (4) 50 sec, (5) 40 sec, (6) 30 sec and (7) 20 sec. The image quality of each series was graded subjectively in a ten-point scale where "1" was given to images with poorest quality and "10" to images with highest quality. Image smoothness, tumour-to-background ratio and background uptake were taken into consideration. Grades 7–10 were given to images with a good or very good quality (appropriate for analysis). Grades 5–6 were given to images with mediocre quality and < 5 to images of poor quality (inappropriate for assessment). A mean grade of 7 was set as a cut-off value for image appropriateness for analysis i.e in the final evaluation only the images with a mean grade ≥ 7 were considered to have quality adequate for assessment. The assessing physicians also measured maximum standardised uptake values (SUVmax) of the liver, mediastinal blood pool (MBP) and three random target lesions.
Phantom Studies

In order to define whether reduced time per bed can be directly translated into reduced radiotracer dose phantom studies were performed. A NEMA phantom, a water phantom (GE Healthcare, Chicago, Illinois, US) and a syringe source were used. The NEMA and water phantoms were filled with an activity of 32.3 MBq and 56.1 MBq and then scanned (using the same Discovery IQ PET/CT system) for 2 min, 1.5 min and 1 min to measure the number of total prompts (depending on the time per bed). Three syringe sources were filled with initial activities of 97.3 MBq, 56.2 MBq and 57.9 MBq and then scanned after 44 min and 109 min which imitated a 25% and a 50% dose reduction, respectively. The number of total prompts measured was then compared with an estimated number to verify the correlation between the dose and the total prompts number.

Statistical Analysis

SPSS Statistics 25 software (Armonk, New York, US) was used for the statistical analysis. Descriptive analysis was performed by calculating mean, median, standard deviation and range. Cohen’s kappa was used for inter-observer agreement in ranking. The intraclass correlation coefficient (ICC[3;1]) was used to calculate the inter-observer agreement for each series. A p value < 0.05 was considered significant.

Results

No adverse effects were observed after 18F-FDG injection. Patients did not report any alarming symptoms.

The mean and median grade values for image quality were highest for series with longest acquisition time and decreased with decreasing time per bed (Fig. 1). Series 1 (2 min per bed) received highest points from all three observers, followed by series 2, then series 3, etc. which resulted in the final ranking as shown in Table 2. The interobserver agreement in ranking was excellent (100%) with kappa coefficient of 1.00 (95% CI [0.83–1.0]). According to all three observers only the series with 2 min and 1.5 min acquisition time (series 1 and 2, respectively) were appropriate for assessment (mean mark ≥ 7).

Table 2

| SERIES | OBSERVER 1 | OBSERVER 2 | OBSERVER 3 |
|--------|------------|------------|------------|
|        | MN         | SD         | MDN        | NO. OF GRADES | PTS | RANK | MN         | SD         | MDN        | NO. OF GRADES | PTS | RANK | MN         | SD         | MDN        | NO. OF GRADES | PTS |
| 2 min  | 8.52       | 1.2        | 9          | 82         | 7   | 1.    | 9.52       | 0.8        | 10         | 85         | 7   | 1.    | 9.03       | 0.9        | 9          | 86         | 7   |
| 1.5 min| 7.95       | 1.5        | 8          | 86         | 6   | 2.    | 7.79       | 1          | 8          | 85         | 6   | 2.    | 8.1        | 1.1        | 8          | 89         | 6   |
| 1 min  | 6.46       | 2          | 6          | 83         | 5   | 3.    | 6.56       | 1.1        | 7          | 88         | 5   | 3.    | 6.66       | 1.2        | 7          | 87         | 5   |
| 50 sec | 5.53       | 2.1        | 5.5        | 86         | 4   | 4.    | 5.57       | 1.3        | 6          | 88         | 4   | 4.    | 5.8        | 1.3        | 6          | 89         | 4   |
| 40 sec | 4.5        | 2          | 4          | 84         | 3   | 5.    | 4.77       | 1.2        | 5          | 84         | 3   | 5.    | 4.64       | 1.4        | 4          | 88         | 3   |
| 30 sec | 3.01       | 1.5        | 3          | 84         | 2   | 6.    | 3.65       | 1.1        | 4          | 86         | 2   | 6.    | 3.39       | 1.3        | 3          | 87         | 2   |
| 20 sec | 2.28       | 1.7        | 2          | 82         | 1   | 7.    | 2.81       | 1.1        | 3          | 81         | 1   | 7.    | 2.59       | 1.4        | 2          | 86         | 1   |

The general intraclass correlation coefficient was very high (0.945, 95% CI [0.936–0.952]) and was the higher the shorter the time per bed (Table 3, Fig. 2). In the phantom study we observed that decreasing time per bed was directly proportional to the decrease in total prompts – a 25% decrease in acquisition time (from 2 min to 1.5 min) resulted in a likewise decrease in total prompts number (Table 4). Phantom studies with the use of the three syringe sources showed the number of total prompts decreased directly proportionally to the administered dose – a 25% dose reduction resulted in a 25% reduction in the total prompts number. The difference in the number of estimated and measured total prompts was ± 5% (Table 5). We observed that SUVmax values measured in the liver, MBP and target lesions were decreasing the longer the time per bed. The target-to-liver and target-to-MBP ratios increased when time per bed was increased (Fig. 3, Supplement Table 1)
Table 3
The inter-observer agreement for each PET series.

| Series  | ICC  | 95%CI LL | 95%CI UL |
|---------|------|----------|----------|
| 2 min   | 0,500| 0,279    | 0,662    |
| 1.5 min | 0,628| 0,463    | 0,749    |
| 1 min   | 0,727| 0,606    | 0,816    |
| 50 sec  | 0,713| 0,586    | 0,805    |
| 40 sec  | 0,777| 0,677    | 0,850    |
| 30 sec  | 0,834| 0,761    | 0,887    |
| 20 sec  | 0,859| 0,795    | 0,905    |
| Total   | 0,945| 0,936    | 0,952    |

ICC – intra-class correlation coefficient, CI – confidence interval; LL – lower limit; UL – upper limit

Table 4
Total prompts measured in the NEMA and water phantoms for three different acquisition times – 2 min, 1.5 min and 1 min.

| Time per bed | Total prompts (NEMA phantom) | Total prompts (water phantom) |
|--------------|------------------------------|------------------------------|
| 2 min        | $4.66 \times 10^7$           | $1.49 \times 10^8$           |
| 1.5 min      | $3.5 \times 10^7$ (24.9% decrease) | $1.12 \times 10^8$ (24.8% decrease) |
| 1 min (50% decrease) | $2.34 \times 10^7$ (49.8% decrease) | $7.40 \times 10^7$ (50.3% decrease) |

Table 5
Decrease in 18F-FDG activity and number of total prompts in time.

| No. of syringe | 18F-FDG activity after time (% decrease) | No. of total prompts measured after time (% decrease) |
|----------------|-----------------------------------------|-----------------------------------------------------|
| 0 min          | 44 min                                  | 109 min                                              |
| 1              | 97.3 MBq                                | 72.0 MBq (26%)                                       |
|                | 47.6 MBq (51.1%)                        |                                                     |
|                | 9.88 $\times 10^8$ (26.1%)              |                                                     |
|                | 7.3 $\times 10^8$ (26.1%)               |                                                     |
|                | 4.54 $\times 10^8$ (54%)                |                                                     |
| 2              | 56.2 MBq                                | 44.1 MBq (21.5%)                                     |
|                | 25.9 MBq (53.9%)                        |                                                     |
|                | 5.29 $\times 10^8$ (26.3%)              |                                                     |
|                | 3.9 $\times 10^8$ (26.3%)               |                                                     |
|                | 2.59 $\times 10^8$ (51%)                |                                                     |
| 3              | 57.9 MBq                                | 43.9 MBq (24.2%)                                     |
|                | 28.9 MBq (50.1%)                        |                                                     |
|                | 5.26 $\times 10^8$ (26.8%)              |                                                     |
|                | 3.85 $\times 10^8$ (26.8%)              |                                                     |
|                | 2.40 $\times 10^8$ (54.4%)              |                                                     |

**Discussion**

In our study we aimed to determine the maximum 18F-FDG dose reduction on a BGO PET/CT camera that would not compromise the image quality. The minimum feasible dose was defined by proxy – we checked if reduction of acquisition time can be directly translated into dose reduction. We showed that there is a linear correlation between time per bed, administered activity and number of total prompts detected by the scanner. Hence, we demonstrated that time per bed reduction is directly proportional to dose reduction. In visual analysis we reported that time per bed can be safely reduced by 25% (from 2 min to 1.5 min) without significant compromise in image quality (only 2 min and 1.5 min scans received a mean grade $\geq 7$). This in turn could be translated into a 25% tracer dose reduction – from 3.0 to 2.25 MBq/kg. We reported that administration of a reduced dose with 2 min time per bed acquisition is a feasible protocol that does not compromise the image quality.

The radiation dose reduction from PET/CT scans can be achieved by optimising either PET or CT scanning protocols. It has been robustly shown that various alterations in CT protocols may cut the used radiation by as much as 1/3 (from 8.1 mSv to 5.5 mSv) [11]. On the other hand, the literature on the radiotracer activity reduction is rather scant.
According to the European Association of Nuclear Medicine (EANM) recommendations the minimum administered activity for a gamma camera like we used in the study (with ≤ 30% bed overlap) and a 2 min time per bed should be 7 MBq/kg. The guidelines also state that the dose can be lowered for PET/CT systems with higher sensitivity or improved performance [3]. In our institution—accordingly to national regulations, instructions from the producer of our PET/CT system, available literature and our personal experience—we routinely administer activities of about 3.7 MBq/kg with acquisition time of 1.5 min [12, 13].

Experimentally, for the purpose of the study, we have reduced the administered dose to 3.0 MBq/kg. We show that further reduction to 2.25 MBq/kg with 2 min acquisition time might be feasible. It is in accordance with a study performed on the same type of scanner (GE Discovery IQ) that showed similarly high sensitivity and performance of the camera after the injection of 2.5 MBq/kg of 18F-FDG. High sensitivity of the scanner was achieved by adopting several technological solutions such as the 3-dimensional mode, extension of the axial field of view (FOV) and increasing number of detector rings from 2 to 5 along FOV [14, 15]. The system also uses a new reconstruction algorithm (Bayesian penalised likelihood algorithm named Q.Clear) that improves signal-to-noise ratio and standardised uptake value (SUV) quantification. In Q.Clear the noise suppression is controlled by a penalty term beta (the only one user-adjusted term in the algorithm). The algorithm also incorporates point-spread-function modelling [16–18].

Prieto et al. showed that average 18F-FDG dose reduction of 23.4% (down to 3.57 MBq/kg) is feasible without significant impairment of image quality. Yet, the study was performed on a 4-ring lutetium oxyorthosilicate PET/CT scanner [19]. On the other hand, Murray et al. reported that emission scans as short as 15 sec per bed position sufficiently identified tumour lesions for quantification. The scans were performed on a Gemini TF PET/CT system after injection of 269–411 MBq of 18F-FDG (3.8–5.9 MBq for a 70 kg patient) [20]. As shown, contemporary PET/CT technology allows for a notable reduction of radiotracer doses compared to the current guidelines.

The findings of this study have to be seen in light of some limitations. First, the research focused on a single clinical condition – Hodgkin lymphoma. It is highly probable that a 25% dose reduction would also be feasible in other aggressive, FDG-avid lymphomas and malignancies yet it may not be so in case of indolent tumours. Hence, further research on more heterogenous groups of patients is needed to explore this subject. Our research is a retrospective study and might show some of method’s inherent limitations such as selection bias or confounding.

Conclusions

In a BGO PET/CT scanner 18F-FDG doses as low as 2.25 MBq/kg are feasible when Hodgkin lymphoma patients are concerned. The reduced dose is especially important in this setting because HL patients undergo multiple PET/CT examinations throughout the clinical process.

Declarations

COMPLIANCE WITH ETHICAL STANDARDS

FUNDING:

No funding was received for conducting this study.

CONFLICT OF INTEREST:

The authors have no relevant financial or non-financial interests to disclose.

ETHICAL APPROVAL:

All procedures performed in this study were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

INFORMED CONSENT:

Informed consent was obtained from all individual participants included in this study.

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