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Original

Optimal activity of [^{18}F]FDG for Hodgkin lymphoma imaging performed on PET/CT camera with BGO crystals

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Abstract

Background: We aimed to find the minimum feasible activity of fluorodeoxyglucose ([^{18}F]FDG) in positron emission tomography/computed tomography (PET/CT) of Hodgkin lymphoma patients performed on a camera with bismuth germanate (BGO) crystals.

Material and methods: Ninety-one [^{18}F]FDG PET/CT scans (each in seven Bayesian Penalized Likelihood [BPL] reconstructions with varying acquisition time per bed position — 2 min, 1.5 min, 1 min, 50 s, 40 s, 30 s, and 20 s) were independently assessed by three physicians to evaluate image quality. Mean administered activity was 3.0 ± 0.1 MBq/kg and mean uptake time was 54.0 ± 8.7 min. The series quality was subjectively marked on a 1–10 scale and then ranked 1–7 based on the mean mark. Interobserver rank correlation and intraclass correlation within each series for the three observers were calculated. Phantom studies were also performed to determine if reduced acquisition time can be directly translated into a reduced activity.

Results: Time series were marked and ranked unanimously — the longer the time of acquisition the higher the mark and rank. The interobserver agreement in the ranking was excellent (100%) with a kappa coefficient of 1.00 (95% CI [0.83–1.0]). The general intraclass correlation coefficient (agreement between the marks observers gave each time series) was very high (0.945, 95% CI [0.936–0.952]) and was higher the shorter the time per bed. According to all three observers only the series with 2 min and 1.5 min acquisition time were appropriate for assessment (mean mark ≥ 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, a reduction of acquisition time of 25% (from 2 min to 1.5 min) could be directly translated into a 25% activity reduction (from 3.0 to 2.25 MBq/kg).

Conclusions: In patients with HL, [^{18}F]FDG activity can be reduced by up to 25% when using a BGO crystal camera, without substantial impact on image quality.

KEY words: activity reduction; [^{18}F]FDG; PET/CT; Hodgkin lymphoma; BGO

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Introduction

The dual-modality positron emission tomography/computed tomography (PET/CT) is nowadays a primary imaging method for a wide range of oncologic, cardiologic, and neurologic diseases. It is used at various stages of the treatment process—from diagnosis and primary staging to treatment response assessment [1–4].

Despite its many advantages, PET/CT is a diagnostic method associated with notable radiation exposure and that may raise concern. During a PET/CT scan patients receive radiation both from the radiotracer and from the CT. The effective dose of the 18F-2-fluoro-2-deoxy-D-glucose ([^{18}F]FDG) PET/CT may reach 25–30 mSv, depending on the CT protocol (high-dose diagnostic

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CT vs low-dose CT for anatomic localization); the radiotracer activity (the effective dose of 18F-FDG is 0.019 mSv/MBq); the anatomical region; and the number of body parts imaged [5–7].

According to the guidelines (based on phantom experiments, theoretical estimations, and retrospective studies on heterogenous populations), the administered activity of [^{18}F]FDG should be 3.5–7 MBq/kg [8–13]. Currently, however, activities smaller than 4.0 MBq/kg are usually injected. In order to comply with the ALARA principle, which states that the activity administered should be As Low As Reasonably Achievable, PET/CT protocols are constantly optimized 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 minimize 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 penalized likelihood (BPL), increase acquisition time per bed, and, finally, reduce the injected activity [8, 10, 14, 15].

The aim of the study was to determine the minimum feasible [^{18}F]FDG activity 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.

Material and methods

Patients

We retrospectively evaluated 18F-FDG PET/CT scans of patients with Hodgkin lymphoma (HL) referred to the Dolnoslaskie Affidea PET/CT Centre for disease staging or response assessment between January 2017 and October 2018. Patient and PET/CT scan characteristics are summarized in Table 1.

Table 1. Characteristics of patients and performed positron emission/computed tomography (PET/CT) scans

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; MBq — megabecquerels; SD — standard deviation

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 were 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, current modulation, and pitch of 1.375:1. 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. Computed tomography dose index (CTDIvol) ranged from 1.19 to7.02 mGy (depending on patient body mass).

Immediately after CT scanning, a whole-body three-dimensional PET was acquired. The scan range was from the top of the head to the mid-thighs. For each bed position (24% overlap) a 2 min list mode acquisition was used. The images were then reconstructed with a reduced time per bed of 1.5 min, 1 min, 50 s, 40 s, 30 s, and 20 s. The emission data were 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 Penalized Likelihood (Q.Clear) algorithm [16–21]. The matrix size was 256 x 256 and the voxel size 2.73 x 2.73 x 2.78 mm^3. 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 analyzed with GE Healthcare Advantage Workstation (Chicago, Illinois, United States) independently by three experienced nuclear medicine physicians. Each reviewer assessed PET/CT scans in seven-time series (blinded and presented in random order): 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 s, (5) 40 s, (6) 30 s and (7) 20 s. The image quality of each series was graded subjectively on a ten-point scale where "1" was given to images with the poorest quality and "10" to images with the highest quality. Image smoothness, tumor-to-background ratio, and background uptake (measured in the mediastinal blood pool) were taken into consideration. Grades 7–10 were given to images with 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). The assessing physicians also measured maximum standardized 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 activity, phantom studies were performed. A National Electrical Manufacturers Association (NEMA) phantom, a water phantom (GE Healthcare, Chicago, Illinois, US), and a syringe source were used. The NEMA and water phantoms were filled with background 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% activity reduction, respectively. The number of total prompts measured was then compared with an estimated number to verify the correlation between the activity and the total number of prompts.

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

The mean and median grade values for image quality were highest for series with the longest acquisition time and decreased with decreasing time per bed (Fig. 1, Tab. 2). Series 1 (2 min per bed) received the highest points from all three observers, followed by series 2, then series 3, etc. which resulted in the final ranking as shown in Table 1. The interobserver agreement in the ranking was excellent (100%) with a 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).

The general intraclass correlation coefficient was very high (0.945, 95% CI [0.936–0.952]) and was higher the shorter the time per bed (Tab. 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 (Tab. 4).

Phantom studies with the use of the three syringe sources showed the number of total prompts decreased directly proportionally to the administered activity — a 25% activity reduction resulted in a 25% reduction in the total prompts number. The difference in the number of estimated and measured total prompts was ± 5% (Tab. 5).

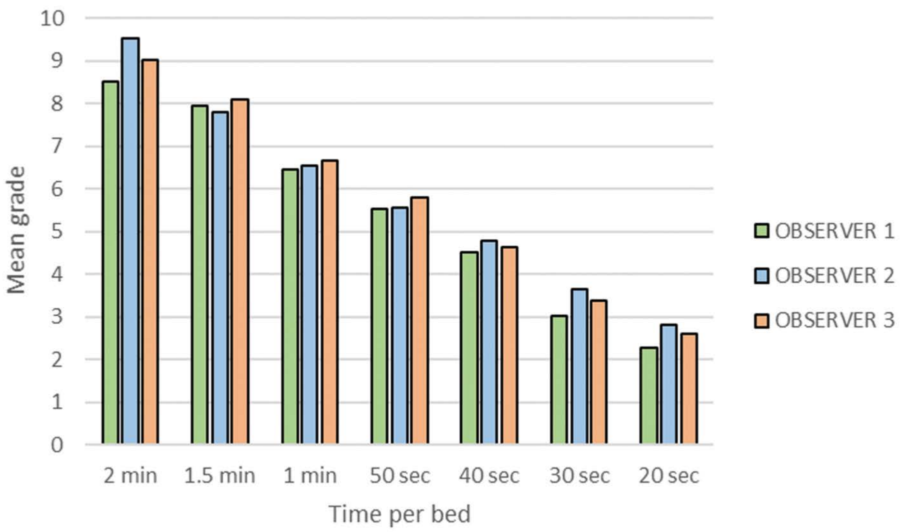

Figure 1. Mean observers' grades for each time per bed series

Table 2. The descriptive statistics of each assessed series (1–7) with their ranks given by the three observers. Series with mean rank ≥ 7 (appropriate for assessment) were highlighted

	OBSERVER 1						OBSERVER 2						OBSERVER 3										
SERIES	MN	SD	MDN	NO. OF GRADES	PTS	RANK	MN	SD	MDN	NO. OF GRADES	PTS	RANK	MN	SD	MDN	NO. OF GRADES	PTS	RANK	SUM OF PTS	3OBS RANK	MEAN RANK	BEST RANK	WORST RANK
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.	21	1.	1.7	1.	1.
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	2.	18	2.	3.0	2.	2.
1 [min]	6.46	2	6	83	5	3.	6.56	1.1	7	88	5	3.	6.66	1.2	7	87	5	3.	15	3.	4.0	3.	3.
50 [s]	5.53	2.1	5.5	86	4	4.	5.57	1.3	6	88	4	4.	5.8	1.3	6	89	4	4.	13	4.	5.0	4.	4.
40 [s]	4.5	2	4	84	3	5.	4.77	1.2	5	84	3	5.	4.64	1.4	4	88	3	5.	9	5.	6.0	5.	5.
30 [s]	3.01	1.5	3	84	2	6.	3.65	1.1	4	86	2	6.	3.39	1.3	3	87	2	6.	6	6.	7.0	6.	6.
20 [s]	2.28	1.7	2	82	1	7.	2.81	1.1	3	81	1	7.	2.59	1.4	2	86	1	7.	3	7.	8.0	7.	7.

MDN — median; MN — mean; PTS — points; SD — standard deviation; 3OBS RANK — final rank from all observers

Table 3. The inter-observer agreement for each positron emission tomography (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 [s]	0.713	0.586	0.805
40 [s]	0.777	0.677	0.850
30 [s]	0.834	0.761	0.887
20 [s]	0.859	0.795	0.905
Total	0.945	0.936	0.952

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

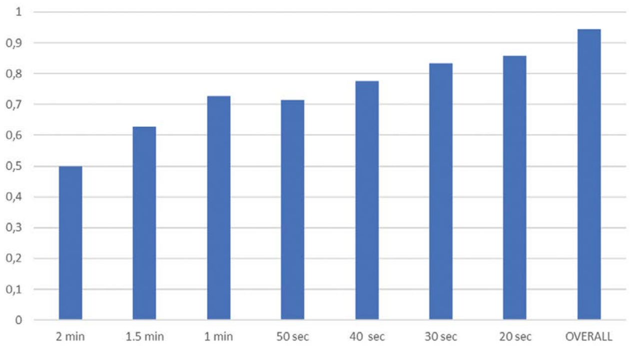

Figure 2. The intra-class correlation coefficient for each PET series; PET — positron emission tomography

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 x 10^7	1.49 x 10^8
1.5 [min] (25% decrease)	3.5 x 10^7 (24.9% decrease)	1.12 x 10^8 (24.8% decrease)
1 [min] (50% decrease)	2.34 x 10^7 (49.8% decrease)	7.40x10^7 (50.3% decrease)

NEMA — National Electrical Manufacturers Association

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, Tab. 6).

Discussion

In our study, we aimed to determine the maximum [^{18}F] FGD activity reduction on a BGO PET/CT camera that would not compromise the image quality. The minimum feasible activity was defined by proxy — we checked if reduction of acquisition time can be directly translated into activity reduction. We showed that there is a linear correlation between time per bed, administered activity, and the number of total prompts detected by the scanner. Hence, we demonstrated that time per bed reduction is directly proportional to activity reduction. In the visual analysis, we reported that a 25% reduction of time per bed (from 2 min to 1.5 min) did not compromise image quality significantly. This in turn could be translated into a 25% tracer activity reduction — from 3.0 to 2.25

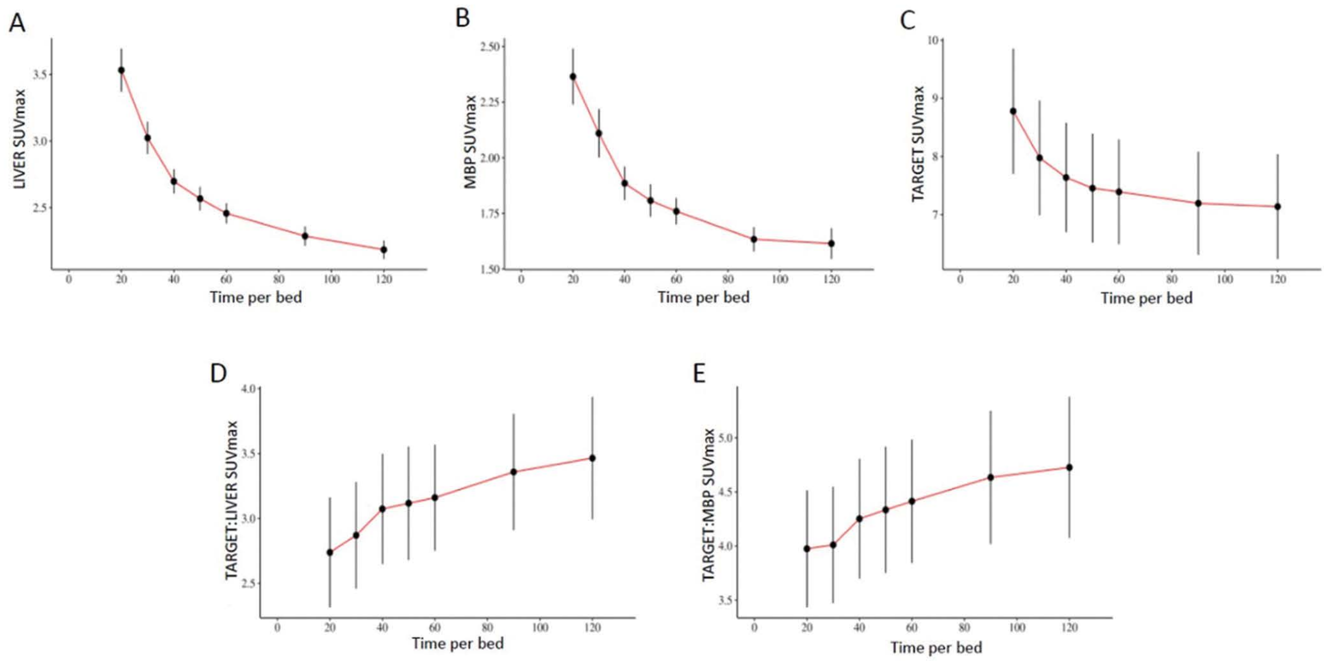

Figure 3. Mean SUVmax values with 95% confidence intervals

Table 5. Decrease in [^{18}F]FDG activity and number of total prompts in time

No. of syringe	[^{18}F]FDG activity after time (% decrease)			No. of total prompts measured after time (% decrease)		
	0 [min]	44 [min]	109 [min]	0 [min]	44 [min]	109 [min]
1	97.3 MBq	72.0 MBq (26%)	47.6 MBq (51.1%)	9.88 x 10^8	7.3x10^8 (26.1%)	4.54 x 10^8 (54%)
2	56.2 MBq	44.1 MBq (21.5%)	25.9 MBq (53.9%)	5.29 x 10^8	3.9x10^8 (26.3%)	2.59 x10^8 (51%)
3	57.9 MBq	43.9 MBq (24.2%)	28.9 MBq (50.1)%	5.26 x 10^8	3.85x10^8 (26.8%)	2.40 x 10^8 (54.4%)

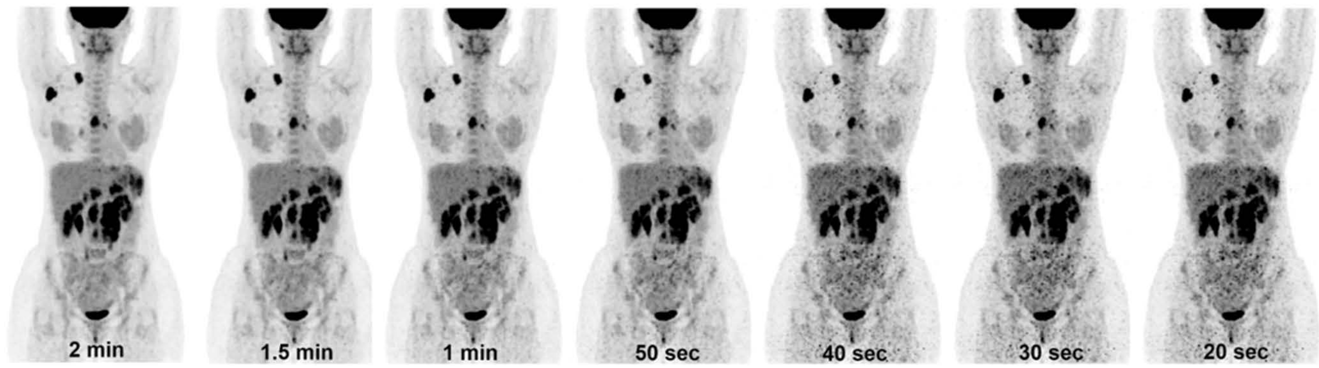

Figure 4. Maximum intensity projection images of the same patient with decreasing time per bed

MBq/kg. We reported that administration of reduced activity 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 optimizing 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) [22].

According to the European Association of Nuclear Medicine (EANM) recommendations, the minimum administered activity for a gamma camera as 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 [8]. In our institution — according 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 an acquisition time of 1.5 min [16, 17].

Experimentally, for the purpose of the study, we have reduced the administered activity to 3.0 MBq/kg. We show that further reduction to 2.25 MBq/kg with 2 min acquisition time might be feasible (Fig. 4). 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 [^{18}F]FDG. The 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 the number of detector rings from 2 to 5 along the FOV [23, 24]. The system also uses a new reconstruction algorithm (Bayesian penalized likelihood algorithm named Q.Clear) that improves signal-to-noise ratio and standardized uptake value (SUV) quantification. In Q.Clear the noise suppression is controlled by a penalty term beta (the only user-adjusted term in the algorithm). The algorithm also incorporates point-spread-function modeling [25–27].

Prieto et al. showed that an average [^{18}F]FDG activity reduction of 23.4% (down to 3.57 MBq/kg) is feasible without significant impairment of image quality [28]. On the other hand, Murray et al. reported that emission scans as short as 15 s per bed position sufficiently identified tumor lesions for quantification. The scans were performed on a Gemini TF PET/CT system after injection of 269–411 MBq of [^{18}F]FDG (3.8–5.9 MBq for a 70 kg patient) [29]. As shown, contemporary PET/CT technology allows for a notable reduction of radiotracer activities compared to the current guidelines.

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

Conclusions

In a BGO PET/CT scanner [^{18}F]FDG activities as low as 2.25 MBq/kg are feasible when Hodgkin lymphoma patients are concerned. The reduced activity is especially important in this setting

Table 6. Maximum standarised uptake values measure in the liver mediastinal blood pool and target lesions

		M	Me	SD	IQR	Min	Max
LIVER SUVmax	20 [s]	3.53	3.40	0.77	0.90	2.10	5.50
	30 [s]	3.02	3.00	0.58	0.80	1.90	5.00
	40 [s]	2.70	2.70	0.44	0.50	1.80	4.00
	50 [s]	2.57	2.60	0.42	0.50	1.70	4.10
	60 [s]	2.46	2.50	0.36	0.40	1.70	3.70
	90 [s]	2.29	2.25	0.35	0.40	1.60	3.20
	120 [s]	2.18	2.20	0.33	0.30	1.60	3.20
MBP SUVmax	20 [s]	2.37	2.30	0.60	0.70	1.20	4.30
	30 [s]	2.11	2.00	0.52	0.50	1.30	3.80
	40 [s]	1.89	1.90	0.36	0.50	1.30	3.10
	50 [s]	1.81	1.80	0.35	0.30	1.10	2.90
	60 [s]	1.76	1.70	0.28	0.30	1.30	2.60
	90 [s]	1.64	1.60	0.26	0.38	1.10	2.40
	120 [s]	1.62	1.60	0.33	0.40	1.00	3.20
TARGET SUVmax	20 [s]	8.78	7.90	4.17	6.12	2.00	23.10
	30 [s]	7.98	7.50	3.82	5.62	2.00	17.70
	40 [s]	7.64	7.23	3.64	5.58	1.90	16.60
	50 [s]	7.45	7.17	3.62	5.57	1.80	16.73
	60 [s]	7.38	6.90	3.47	5.17	1.80	16.07
	90 [s]	7.18	7.10	3.41	5.20	1.50	15.67
	120 [s]	7.12	7.00	3.46	5.30	1.40	15.47
TARGET: LIVER SUVmax	20 [s]	2.74	2.45	1.64	1.59	0.36	11.00
	30 [s]	2.87	2.63	1.59	1.54	0.57	8.70
	40 [s]	3.07	2.83	1.65	2.18	0.66	7.64
	50 [s]	3.12	2.98	1.69	2.15	0.67	7.53
	60 [s]	3.16	2.97	1.58	2.07	0.72	7.74
	90 [s]	3.36	3.07	1.73	2.48	0.71	7.82
	120 [s]	3.46	3.18	1.83	2.51	0.64	7.73
TARGET: MBP SUVmax	20 [s]	3.97	3.38	2.09	2.12	0.69	12.16
	30 [s]	4.01	3.76	2.08	2.94	0.83	9.88
	40 [s]	4.25	3.72	2.14	3.22	1.12	8.94
	50 [s]	4.33	3.94	2.26	3.02	1.00	9.84
	60 [s]	4.41	4.18	2.21	2.96	1.06	9.45
	90 [s]	4.63	4.41	2.39	3.30	1.07	9.79
	120 [s]	4.73	4.35	2.52	3.68	1.00	10.42

M — mean; Me — median; SD — standard deviation; IQR — interquartile range; Min — minimum; Max — maximum; MBP — mediastinal blood pool; SUVmax — maximum standarised uptake value

because HL patients undergo multiple PET/CT examinations throughout the clinical process.

Ethics approval and consent to participate

The research has been performed in accordance with the Declaration of Helsinki and its further amendments. The study has been granted ethics committee approval (Military Medical Chamber Ethics Committee, reference no. 150/17, April 28, 2017). Informed consent was obtained from all study participants.

Consent for publication

Consent for publication was obtained from all study participants.

Availability of data and materials

All data generated or analyzed during this study are included in this published article and its supplementary information files.

Conflict of interest

The authors declare that they have no competing interests.

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The authors received no specific funding for this work.

Authors' contributions

MD designed the study, analyzed the data, and contributed to writing the manuscript. EWP designed the study, collected and analyzed the data, and was the main contributor in writing the manuscript. AG and AM collected and analyzed the data. AP, MK, and MG were the main contributors to the phantom experiments. ZP designed the study and collected the data. MC collected the data. All authors read and approved the final manuscript.

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