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Digital vs. analog PET/CT: intra-subject comparison of the SUVmax in target lesions and reference regions

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Abstract

Purpose The purpose of this study was to assess whether digital photon counting technology in digital PET/CT influences the quantification of SUVmax in target lesions and regions of reference compared to analog PET/CT before an interchangeable use of either system in follow up studies.

Methods From January to June of 2018, 100 oncological patients underwent successive PET/CT imaging with digital and analog systems in the same day. Fifty-eight patients underwent analog imaging first and digital imaging thereafter, and 42 patients the other way round. SUVmax was measured in reference regions (liver and mediastinal blood pool) and in the most metabolically active target lesion in each patient. According to the sequence order of PET/CT acquisition, two groups of SUVmax values were obtained, i.e. group 1: analog PET/CT performed first; group 2: digital PET/CT performed first.

Results Mean SUVmax in the total sample (regardless of the order of PET/CT acquisition) in the target lesions with the analog PET/CT was 8.14 ± 6.39 and the digital 9.97 ± 6.14 ($P = 0.000$). Total mean SUVmax in the liver with the analog was 4.39 ± 2.59 and the digital 4.46 ± 3.18 ($P = 0.477$). Total mean SUVmax in the mediastinal blood pool with the analog was 2.30 ± 0.67 and the digital 2.54 ± 0.74 ($P = 0.000$).

Group 1: mean SUVmax in the target lesions with the analog system was 6.64 ± 4.71 and the digital 9.48 ± 5.60 ($P = 0.000$). Mean liver SUVmax with the analog was 4.70 ± 2.90 and the digital 4.80 ± 3.72 ($P = 0.088$). Mediastinal blood pool SUVmax with the analog was 2.33 ± 0.66 and the digital 2.45 ± 0.73 ($P = 0.041$).

Group 2: mean SUVmax in target lesions with the digital system was 10.63 ± 6.88 and the analog 10.16 ± 7.76 ($P = 0.046$). Mean liver SUVmax with the digital was 3.99 ± 2.20 and the analog 3.96 ± 2.04 ($P = 0.218$). Mediastinal blood pool SUVmax with the digital was 2.66 ± 0.75 and the analog 2.27 ± 0.68 ($P = 0.000$).

No significant differences between both time delays were found.

Conclusions Improved photon counting technology in the digital PET/CT, and the effect of delayed increased uptake and retention significantly increases SUVmax values. This has to be taken into account before interchangeable use of either system in follow up studies.

Keywords Digital PET/CT · Analog PET/CT · SUVmax · Intra-subject comparison

Introduction

The use of digital PET/CT is expected to increase in the following years due to improved image quality, volumetric resolution and sensitivity gains, as well as faster timing resolution compared to analog PET/CT. Such improvements are based on the development of digital photon counting technology, with a 1:1 coupling between scintillation crystal and detector, and a faster time of flight technology [1–7].

Progressive introduction of digital PET/CT will raise the question of whether follow up PET/CT studies can be

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interchangeable between digital and analog systems, especially in oncological patients in whom SUVmax values are often used to evaluate treatment response.

The aim of our study was to assess whether digital photon counting technology in digital PET/CT influences the quantification of SUVmax in target lesions and regions of reference in comparison to analog PET/CT in the same patient. Such comparison is necessary before an interchangeable use of either system in follow-up studies.

Materials and methods

Patient population

One hundred oncological patients were prospectively studied between January and June of 2018. The group consisted of 59 men and 41 women with a mean age of 67 ± 12 years.

All patients underwent successive PET/CT imaging with digital and analog systems in the same day. The analog system was a Philips Gemini TF 64 and the digital a Philips Vereos. In 58 patients the analog study was done first and the digital study thereafter, and in 42 patients the other way round. When the patients came for an initial study, the digital PET/CT was done first. When the patients came for a follow up study, the analog PET/CT was done first as their previous studies had been done with the analog system.

All patients signed an informed consent and the study was approved by the institutional ethical board.

Imaging protocol

The imaging protocol consisted of a single radiotracer injection, calculated to each patient total body weight (0.1 mCi*Kg), after a minimum of 6 h of fasting. In 90 patients the radiotracer used was 18F-FDG (FDG) and in ten patients 18F-Choline. The first PET/CT was performed 60 min after the injection of the radiotracer. The second PET/CT was performed as soon as it was available (depending on laboratory logistics). Mean time delay between both studies was 50 ± 14 min.

The CT component of both scanners is a 64-slice helical multidetector. The CT acquisition parameters for both systems were: 120kVp, tube current modulation, pitch of 0.828, and 3 mm slice thickness (with slice increment of 1.5 mm). No intravenous or oral contrast was used. CT reconstruction was done according to recommended clinical settings for each device: filtered back projection in the analog system and iDose iterative reconstruction in the digital system.

The active field of view (FOV) for the PET was 57.6 cm in both systems. The matrix size for the digital system was 288 × 288 with a 2 mm voxel and for the analog system a 144 × 144 matrix with 4 mm voxel. Axial FOV for the analog system was 18 and 16.4 cm in the digital system. Both studies were acquired with list-mode time of flight (TOF) for 2 min/bed position.

Analog PET image reconstruction was performed using 3 iterations and 33 subsets, 3D ordered subset expectation maximization (3D-OSEM). The reconstruction for the digital PET was decided as the one which produced the best image quality for clinical conditions in the laboratory: two iterations, ten subsets, 3D-OSEM with point spread function (PSF) resolution recovery.

Image analysis

The image analysis was performed using the Philips IntelliSpace Portal 8.0. SUVmax was measured in the standard reference regions (liver and mediastinal blood pool) and in the most metabolically active target lesion in each patient, drawing regions of interest (ROI) of the same size in both studies.

The ROI for the SUVmax in the liver was drawn without including hypermetabolic or hypometabolic lesions. The ROI for the SUVmax in the mediastinal blood pool was drawn on the descending thoracic aorta including the vessel wall. In the studies with more than one possible target lesion, only the one with the highest SUVmax was included. A total of 13 patients did not have any target lesion: eight patients underwent the analog PET/CT first and five patients the digital PET/CT first.

Statistical analysis

Data are presented as mean ± standard deviation. According to the sequence order of PET/CT acquisition, two groups of SUVmax values were obtained, i.e. group 1: analog PET/CT performed first; group 2: digital PET/CT performed first. Normality distribution of SUVmax values was assessed by the Kolmogorov-Smirnov test. Comparison of mean SUVmax of target lesions and reference regions between groups was performed using the Wilcoxon test. A comparison of analog-to-analog and digital-to-digital mean SUVmax between groups 1 and 2 was also performed by the Wilcoxon test. Finally, correlation between acquisition time delay and SUVmax in target lesions was performed by simple linear regression analysis.

P value < 0.05 was considered statistically significant. IBM SPSS Statistics V25 software package was used for all statistical analyses.

Results

Table 1 shows mean SUVmax values of the total sample, regardless of the sequence order of PET/CT acquisition. Mean SUVmax of the target lesions and mediastinal blood pool obtained with the digital system were significantly higher than with the analog system, whereas mean SUVmax of the liver did not significantly differ between both systems.

Table 1 Mean SUVmax values of the total sample and statistical significance

Measure	Mean SUVmax		
	Target lesions	Liver	Mediastinal blood pool
Analog PET/CT	8.14 ± 6.39	4.39 ± 2.59	2.30 ± 0.67
Digital PET/CT	9.97 ± 6.14	4.46 ± 3.18	2.54 ± 0.74
Significance	$P = 0.000$	$P = 0.477$	$P = 0.000$
Mean SUVmax difference	−1.83 ± 3.41	−0.07 ± 0.92	−0.24 ± 0.45
Mean percentage difference	−34.76 ± 39.44	−0.74 ± 12.63	−12.39 ± 21.91

Mean time delay 50 ± 0.015 min

Table 2 shows mean SUVmax values of group 1 (and degree of difference). Mean SUVmax of the target lesions and mediastinal blood pool were significantly higher in the digital system than in the analog one, whereas mean SUVmax of the liver did not significantly differ between both systems (Fig. 1).

Table 3 shows mean SUVmax values of group 2 (and degree of difference). Mean SUVmax of the target lesions and mediastinal blood pool were significantly higher in the digital system than in the analog one, whereas mean SUVmax of the liver did not significantly differ between both systems (Fig. 2).

Table 4 shows the degree of significance of the analog-to-analog and digital-to-digital SUVmax comparison between groups 1 and 2. No significant differences were found between groups except for mean SUVmax in target lesions with the analog PET/CT (group 1 [6.64 ± 4.71] vs group 2 [10.16 ± 7.76]; $p = 0.024$).

Time delay between both studies in group 1 was 50.38 ± 16.31 min, and in group 2 it was 43.71 ± 24.37 min ($P = 0.184$). Simple linear regression analysis (R^2) between acquisition time delay and SUVmax difference in target lesions was 0 in group 1 and 0.29 in group 2.

Discussion

Our results consistently show a higher mean SUVmax value with the digital PET/CT as compared to the analog PET/CT. When the analog PET/CT was done first, significant differences were found in the mean SUVmax of target lesions and mediastinal blood pool between both systems, whereas no significant differences were found in the liver. When the digital PET/CT was done first, we also found significant differences in mean SUVmax of target lesions and mediastinal blood pool, but no significant differences in the liver.

We believe that the higher SUVmax of target lesions in the digital scanner, when the analog study had been done before, was due to the higher sensitivity of the digital system plus the effect of a delayed increased uptake and retention (mean percentage difference −50.93). On the other hand, when the digital PET/CT was done first, the mean SUVmax difference and percentage difference were of lower magnitude, probably because in such situations the effect of a delayed uptake played in favour of the analog system. Nevertheless, a delayed uptake effect was not sufficient to produce higher SUVmax values than the digital PET/CT. Also, the effect of the delayed uptake in the analog system is probably the reason for the significant difference in target lesions of group 1 vs 2 when performing the analog-to-analog comparison.

The reasons why the digital PET/CT has a higher maximum count rate, and thus sensitivity, can be explained by the incorporation of a digital photon count rate, a 1:1 coupling between detectors and scintillation crystals and a faster TOF technology [2–5]. The digital photon counter detector in the digital PET/CT consists of 3200 single photon avalanche diodes (cells). These cells are coupled to a digital photon counter, which produces a binary count from the individual breakdowns of each single photon avalanche

Table 2 Mean SUVmax and statistical significance in group 1

Measure	Mean SUVmax		
	Target lesions	Liver	Mediastinal blood pool
Analog PET/CT	6.64 ± 4.71	4.70 ± 2.90	2.33 ± 0.66
Digital PET/CT	9.48 ± 5.6	4.80 ± 3.72	2.45 ± 0.73
Significance	$P = 0.000$	$P = 0.088$	$P = 0.041$
Mean SUVmax difference	−2.84 ± 3.64	−0.1 ± 1.15	−0.12 ± 0.41
Mean percentage difference	−50.93 ± 40.99	1.98 ± 13.54	−6.76 ± 21.27

Mean time delay 50.38 ± 16.31 min. This group consisted of 58 oncological patients in whom the analog PET/CT was performed first and the digital afterwards, 26 women and 32 men, with a mean age of 67.28 ± 10.43 years
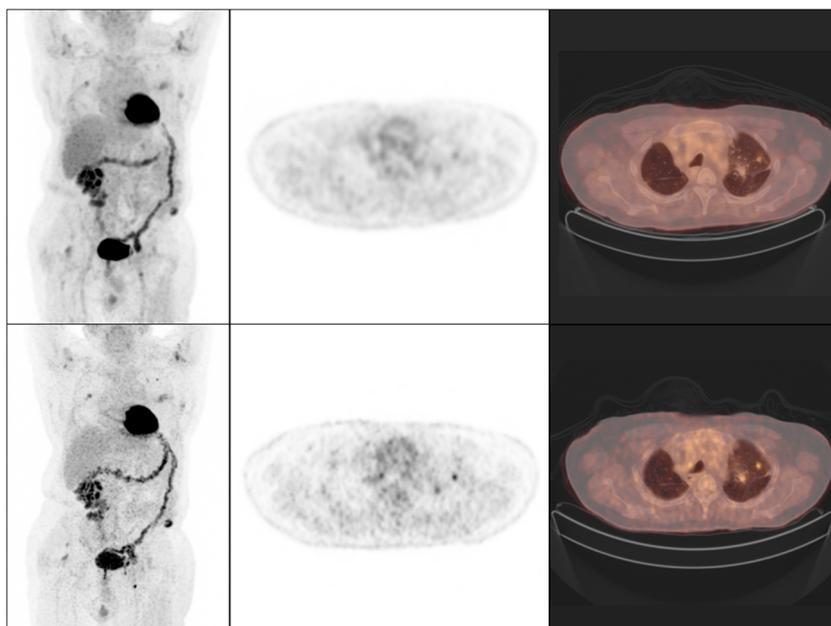
Fig. 1 A 76-year-old male with a retroperitoneal leiomyosarcoma and pulmonary, bone and abdominal metastases, who underwent a follow-up PET/CT. From left to right: MIP, axial PET and axial PET/CT. The *upper row* corresponds to the analog PET/CT (which was done first) and the *lower row* to the digital PET/CT (which was done afterwards). There is a small lung nodule in the left upper lobe that had a SUVmax of 2 with the analog and of 4.97 with the digital system. In this patient, the selected target lesion was a peritoneal implant which had a SUVmax of 6.22 with the analog and a 10.53 with the digital. Liver SUVmax was 4.07 with the analog system and 4.15 with the digital. Mediastinum SUVmax was 2.63 with the analog system and 2.98 with the digital

diode. This technology eliminates the need for the amplification of the readout to produce a summed analog signal and therefore the need of an analog-to-digital processing (required in traditional "analog" PET/CT systems) [3, 5–7]. These changes have achieved a very low dead time, a higher count rate time and thus, a better timing resolution with a higher sensitivity [4, 5].

It is well known that the effect of a delayed increased FDG uptake occurs in tissues with high glycolysis such as tumours that have an increased expression of glucose transporters and hexokinase activity and therefore, an increased production of FDG-6-phosphate which is trapped inside the cells [8, 9]. As more ^{18}F-FDG is captured by the tumour from the interstitial and intravascular activity, more FDG-6-phosphate is synthesized and trapped, thus increasing the SUVmax [8, 9].

However, it is also known that delayed increased FDG uptake does not occur in all tumours. Tumour heterogeneity

such as proliferation rate, hypoxia and blood flow play a part in the effect of a delayed uptake. Tumours with an initial low FDG uptake show less prominent delayed increased uptake. This has been proven for breast, small lung nodules and some pancreatic cancers [8]. Thus, some of our findings may not have been influenced by imaging time and can only be explained by differences in technology detection.

Delayed increased uptake of 18F-Choline has also been reported in malignant lesions of prostate cancer [10–14] as seen with the ten prostate cancer patients included in our analysis. Oprea-Lager et al. studied lymph node uptake in 25 prostate cancer patients by early and delayed imaging and later assessed the malignancy by histopathology and/or follow-up studies. All of the benign nodes showed a decreased uptake, whereas 95% of the pelvic lymph nodes assessed as malignant showed a stable or increased uptake. They suggest that this pattern can be used as an indicator of

Table 3 Mean SUVmax and statistical significance in group 2

Measure	Mean SUVmax		
	Target lesions	Liver	Mediastinal blood pool
Analog PET/CT	10.16 ± 7.76	3.96 ± 2.04	2.27 ± 0.68
Digital PET/CT	10.63 ± 6.88	3.99 ± 2.20	2.66 ± 0.75
Significance	$P = 0.046$	$P = 0.218$	$P = 0.000$
Mean SUVmax difference	-0.47 ± 2.55	0.04 ± 0.48	0.40 ± 0.46
Mean percentage difference	7.68 ± 18.77	-0.42 ± 12.76	13.79 ± 19.07

Mean time delay 43.71 ± 24.37 min. This group consisted of 42 oncological patients in whom the digital PET/CT was performed first and the analog afterward; 15 women and 27 men, with a mean age of 66.52 ± 13.32 years

Fig. 2 A 53-year-old female with a pulmonary adenocarcinoma who underwent an initial staging PET/CT. From left to right: MIP, axial PET and axial PET/CT. The *upper row* corresponds to the digital PET/CT (which was done first) and the *lower row* to the analog PET/CT (which was done afterwards). A primary pulmonary lesion (target lesion) in the right lower lobe that had a SUVmax of 26.70 with the digital system and 26.36 with the analog system. Liver SUVmax was 3.71 with the digital system and 3.65 with the analog. Mediastinum SUVmax was 2.94 with the digital system and 2.85 with the analog
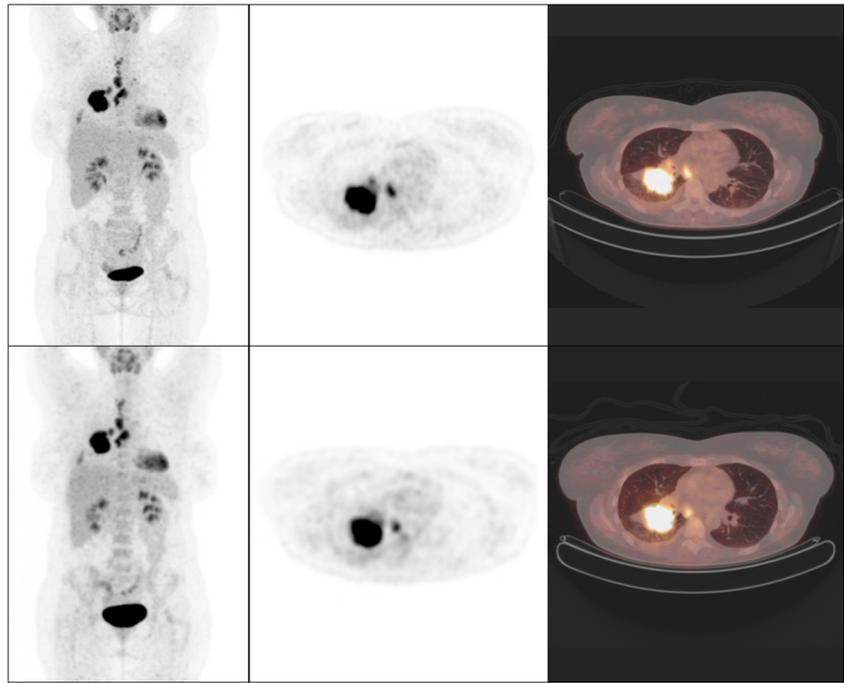
malignancy with a positive predictive value of 97% [10]. Similar findings were reported in a study of Beheshti et al., where false positive lymph nodes showed a rapid washout on the dynamic images and a decreased SUVmax in delayed images, whereas malignant lymph nodes showed a constant or increased uptake pattern [11]. Finally, Kwee et al. found that dominant malignant regions in the prostate (histologically proven after prostatectomy) showed a significant increase of SUVmax between initial and delayed scans [12].

Because the digital PET/CT is a recent technology, there are few studies comparing it with the traditional analog PET/CT systems. Nguyen et al. studied 21 oncological patients, with a total of 52 representative lesions. All of them underwent the analog PET/CT first and the digital afterwards. They found that the SUVmax difference in the representative lesions was 36% higher for the digital system [4]. This is similar to our findings, where the SUVmax difference values were also higher with the digital system. The aforementioned study did not find a statistical association between the SUVmax difference (comparing GeminiTF and Vereos systems) and acquisition time delay [4]. Likewise we did not find any statistical association with the acquisition time delay

when the analog PET/CT was performed first ($R^2 = 0$). When the digital PET/CT was performed first, we found only a very small association ($R^2 = 0.29$) between acquisition time delay and the SUVmax difference in target lesions. To our knowledge, there are no studies where the digital PET/CT is performed first.

Chin et al. studied the SUV changes in normal tissue imaging at 1 and 3 h post FDG injection in 99 patients [9]. They found no significant activity differences in liver and lung over time, hypothesizing that the absence of significant differences could be due to an integrated similar compartmental influx-efflux [9]. It could also be that the high levels of glucose-6-phosphatase in the liver should result in a reduction in the levels of FDG-6-phosphate that it contains. This could also explain our findings in the liver, where no significant differences were found between systems or acquisition times.

Even though the difference of the mean SUVmax in mediastinal blood pool was not very high, we did find significant differences between both systems. Despite vascular activity being expected to decrease in time due to the continuous clearance of FDG by the kidneys [8, 9, 15], the SUVmax was always higher with the digital system (regardless of the sequence order of PET/CT acquisition). This finding might be in part explained by the better resolution and count rate of the vessel wall by the digital PET.

The main limitation of our study is the impossibility of doing both studies at the same time, so the influence of delayed increased uptake cannot be ruled out. Another limitation is the use of a different number of iterations during the image reconstruction. With higher iterations, noise increases and therefore the SUVmax also increases [16–18]. Nevertheless, the analog PET/CT was the one which used more iterations and that did not result

Table 4 Degree of significance of analog-to-analog and digital-to-digital SUVmax comparison between groups 1 and 2

Measure	Statistical significance		
	Target lesions	Liver	Mediastinal blood pool
Analog PET/CT	$P = 0.024$	$P = 0.179$	$P = 0.323$
Digital PET/CT	$P = 0.531$	$P = 0.577$	$P = 0.771$

in a higher SUVmax. In addition, point spread function modelling was used in the reconstruction algorithm with the digital PET/CT. This reconstruction algorithm is known to improve signal-to-noise ratio and lesion detectability, but it also can increase the SUVmax, especially in small lesions [18, 19]. Finally, this is a heterogeneous series of patients with various primary tumours, disease stage and treatment conditions. Furthermore, ten studies were done with Choline, which increases the heterogeneity of the sample. Although this small group of patients studied with Choline does not allow a proper separate statistical analysis, a similar trend to FDG was observed, which indicates that the increased SUVmax obtained in the digital system is not limited to FDG. Future comparisons in more selected groups of patients may bring additional information on the relative advantages and performance of the digital vs analog PET/CT.

Conclusion

Improved photon counting technology in the digital PET/CT, and the effect of delayed increased uptake and retention significantly increases SUVmax values. This has to be taken into account before interchangeable use of either system in follow up studies.

Compliance with ethical standards

Conflict of interest All authors declare no conflicts of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or 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 the study.

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