Comparison of Image Quality and Spatial Resolution Between ^{18}F , ^{68}Ga and ^{64}Cu Phantom Measurements Using a Digital Biograph Vision PET/CT

Anja Braune (✉ anja.braune@uniklinikum-dresden.de)

University Hospital Carl Gustav Carus: Universitätsklinikum Carl Gustav Carus <https://orcid.org/0000-0001-7707-9413>

Liane Oehme

University Hospital Carl Gustav Carus: Universitätsklinikum Carl Gustav Carus

Robert Freudenberg

University Hospital Carl Gustav Carus: Universitätsklinikum Carl Gustav Carus

Frank Hofheinz

Helmholtz-Zentrum Dresden-Rossendorf

Jörg van den Hoff

Helmholtz-Zentrum Dresden-Rossendorf

Jörg Kotzerke

Universitätsklinikum Dresden: Universitätsklinikum Carl Gustav Carus

Sebastian Hoberück

University Hospital Carl Gustav Carus: Universitätsklinikum Carl Gustav Carus

Research Article

Keywords: PET/CT, ^{18}F -FDG, ^{68}Ga , ^{64}Cu , NEMA PET Body phantom, Jaszczak phantom, spatial resolution, image quality

Posted Date: January 14th, 2022

DOI: <https://doi.org/10.21203/rs.3.rs-1159557/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Background: The PET nuclide and reconstruction method can have a considerable influence on spatial resolution and image quality of PET/CT scans, which can, for example, influence the diagnosis in oncology. The individual impact of the positron energy of ^{18}F , ^{68}Ga and ^{64}Cu on spatial resolution and image quality of PET/CT scans acquired using a clinical, digital scanner was compared. Furthermore, the impact of different reconstruction parameters on image quality and spatial resolution was evaluated for ^{18}F -FDG PET/CT scans acquired with a scanner of the newest generation.

Methods: PET/CT scans of a Jaszczak phantom and a NEMA PET body phantom, filled with ^{18}F -FDG, ^{68}Ga -HCl and ^{64}Cu -HCl, respectively, were performed on a Siemens Biograph Vision. Images were assessed using spatial resolution and image quality (Recovery Coefficients (RC), coefficient of variation within the background, Contrast Recovery Coefficient (CRC), Contrast-Noise-Ratio (CNR), and relative count error in lung insert). In a subsequent analysis, the scan of the NEMA PET body phantom filled with ^{18}F -FDG was reconstructed applying different parameters (with/without the application of Point Spread Function (PSF), Time of Flight (ToF) or post-filtering; matrix size). Spatial resolution and quantitative image quality were compared between reconstructions.

Results: We found that image quality was comparable between ^{18}F -FDG and ^{64}Cu -HCl PET/CT measurements featuring similar maximal endpoint energy. In comparison, RC, CRC and CNR were worse in ^{68}Ga -HCl data, despite similar count rates. Spatial resolution was up to 18 % worse in ^{68}Ga -HCl compared to ^{18}F -FDG images. Post-filtering of ^{18}F -FDG acquisitions changed image quality the most and reduced spatial resolution by 52 % if a Gaussian filter with 5 mm FWHM was applied. ToF measurements especially improved the recovery of the smallest lesion ($\text{RC}_{\text{mean}} = 1.07$ compared to 0.65 without ToF) and improved spatial resolution by 29 %.

Conclusions: The positron energy of PET nuclides influences spatial resolution and image quality of digital PET/CT scans. Image quality of ^{68}Ga -HCl PET/CT images was worse compared to ^{18}F -FDG and ^{64}Cu -HCl, respectively, despite similar count rates. Reconstruction parameters have a high impact on image quality and spatial resolution and should be considered when comparing images of different scanners or centers.

Background

Currently, different radiotracers are available for the examination of the same disease, like ^{18}F -PSMA-1007 and ^{68}Ga -PSMA-11 for the diagnosis of prostate cancer (1–3) or ^{68}Ga -DOTA-TOC and ^{18}F -SiFAlin-TATE for the diagnosis of neuroendocrine tumors (4). It was reported in a clinical study examining 102 patients, that in repeated measurements of the same patient using the same PET/CT scanner, ^{18}F -PSMA-1007-PET revealed about 5 times as many PSMA-positive lesions attributed to benign origin as did ^{68}Ga -PSMA-11-PET (1, 2). The same study revealed that the maximal Standardized Uptake Value (SUV_{max}) of

lesions attributed to benign origin was higher for ^{18}F -PSMA-1007-PET compared to ^{68}Ga -PSMA-11-PET (2). It is currently unclear whether these differences are due to different biokinetics and affinities of the tracers (5), different counting statistics in the respective measurements or whether different physical properties increase detection probability. The maximum positron energy and thus the mean range in tissue differ between ^{18}F and ^{68}Ga : positrons arising from the decay of ^{68}Ga feature a three times higher endpoint energy than that of ^{18}F and therefore have a much greater mean range in tissue (3.5 mm compared to 0.6 mm) (Table 1). This reduces spatial resolution of ^{68}Ga -PET.

The individual impact of different physical properties of PET nuclides has been investigated in detail for preclinical PET/CT scanners featuring higher intrinsic spatial resolution (6, 7). However, it is not yet known whether the different positron energies of ^{68}Ga and ^{18}F are recognizable in images acquired with clinical PET/CT scanners of the newest generation, enabling Time of Flight (ToF) measurements and Point Spread Function (PSF) reconstruction.

Therefore, the aim of this work was to compare the individual impact of the positron energy of the most commonly used PET isotopes ^{18}F and ^{68}Ga , as well as ^{64}Cu , on image quality and spatial resolution of scans acquired with a clinical, digital PET/CT scanner. This study focused specifically on the influence of positron energy, since even an adjustment of the amount of the injected radioactivity or acquisition duration cannot compensate for this physical property. Therefore, all factors that could influence the image quality in addition to the positron energy were kept comparable (count rate, PET device, phantom setup, reconstruction parameters). The scans were recorded with one of the latest digital PET/CT scanner with high spatial and temporal resolution, so that image deterioration is to be expected due to the increased positron range of ^{68}Ga .

In a subsequent investigation, the impact of different reconstruction parameters on spatial resolution, image quality and SUV were investigated for ^{18}F -FDG PET/CT examinations performed with the newest scanner generation. This is of importance to be able to compare clinical data with other scanners or the previous models, especially since it has been suggested to define cut-off values for the classification of malignancy of bone metastasis in ^{18}F -PSMA-1007 PET/CT (8). Since these values are meant to be used for investigations in different clinics, in which different reconstruction protocols are used, the individual influence of different reconstruction parameters on quantitative image parameters must be assessed.

Methods

A Jaszczak phantom (Model ECT/DLX/P, Data Spectrum Corporation, Durham, USA), featuring cold rods (4.8 mm to 12.7 mm in diameter) and spheres (9.5 mm to 31.8 mm in diameter) surrounded by an activity-filled background compartment (0.3 mol HydroChloric acid (HCl)), was used in order to qualitatively evaluate spatial resolution and image quality. In a subsequent measurement, quantitative assessment of image quality and spatial resolution was performed using the NEMA PET Body phantom (PTW Freiburg), which allows hot spot imaging of spheres of different sizes (10 mm to 37 mm in

diameter) at different sphere-to-background contrast ratios. All measurements were performed on a digital Biograph Vision PET/CT system (Siemens Healthineers).

Qualitative Evaluation of Spatial Resolution

The background compartment of the Jaszczak phantom was filled with ^{18}F -FDG, ^{68}Ga -HCl and ^{64}Cu -HCl, respectively, aiming at an activity concentration of 5.3 kBq/mL. Following a low dose CT (120 kVp, 78 mAs, spiral pitch factor of 1.5, 512 x 512 matrix with a pixel size of 0.98 mm x 0.98 mm) used for attenuation correction of the following PET scan, a static PET scan was acquired in list mode over one bed position, covering an axial Field of View (FoV) of 26.3 cm. PET data were reconstructed according to the standards in our clinical routine for ^{18}F -FDG using an Ordered Subset Expectation Maximization (OSEM) 3D iterative reconstruction algorithm with 6 iterations and 5 subsets (6i5s), applying PSF and ToF (TrueX algorithm), into an image matrix size of 440 x 440, resulting in a voxel size of (1.65 x 1.65 x 1.5) mm. No post-filtering was applied (allpass). Reconstructions were performed with attenuation correction and absolute (^{68}Ga) or relative scatter correction (^{18}F ; ^{64}Cu).

In order to achieve comparable counting statistics, reconstructed imaging time was determined based on the recommendations in the NEMA NU 2-2018 protocol for image quality measurements (5.3 kBq/ml at the timepoint of imaging; 30 min emission scan for 100 cm total axial imaging distance), considering the actual activity concentration in the phantom at the timepoint of imaging, the axial FoV and the respective decay probability (Table 1). Resulting reconstructed imaging times were 546 sec, 611 sec and 2629 sec for ^{18}F , ^{68}Ga and ^{64}Cu , respectively.

For qualitative evaluation of the Jaszczak phantom scans, the smallest resolvable rod and sphere were determined.

Table 1
Physical properties of the positron emission radioisotopes ^{18}F , ^{68}Ga and ^{64}Cu (9).

	^{18}F	^{68}Ga	^{64}Cu
β + yield (%)	96.7	88.0 (1899 keV) 1.1 (822 keV)	17.4
Half-life (min)	109.8	67.6	762
Max. end-point β + energy	633.5	1899.1	653.1
Average β + energy	249.3	836.0	278
Maximum range of positrons in water (mm)	2.4	9.2	2.5
Mean range of positrons in water (mm)	0.6	3.5	0.7

Quantitative Evaluation of Image Quality

The NEMA PET Body phantom was filled with ^{18}F -FDG, ^{64}Cu -HCl and ^{68}Ga -HCl, respectively. According to the recommendations in the NEMA NU 2-2018 protocol, we aimed at an activity concentration of 5.3 kBq/ml in the background compartment and a sphere-to-background activity concentration ratio of 4:1 and 8:1, respectively. The actual activity concentrations at the timepoint of imaging are specified in Table 2.

Table 2
Activity concentration at start of imaging and detected total number of true events.

Nuclide	Weight setup	Sphere-back-ground activity concentration ratio	Activity concentration in spheres (kBq/ml)	Activity concentration in background compartment (kBq/ml)	Total number of true events ($\times 10^6$ counts)
^{18}F -FDG	normal weight	4.0	18.21	4.51	70.8
	obese	4.0	15.55	3.85	45.0
	normal weight	9.7	51.97	5.35	72.4
	obese	9.7	43.59	4.48	45.0
^{68}Ga -HCl	normal weight	4.3	18.75	4.40	71.3
	obese	4.3	14.63	3.43	44.0
	normal weight	9.4	40.65	4.32	69.9
	obese	9.4	31.52	3.35	44.7
^{64}Cu -HCl	normal weight	5.4	27.70	5.12	72.2
	obese	5.4	26.18	4.84	45.0
	normal weight	8.1	42.16	5.19	71.6
	obese	8.1	40.04	4.93	44.6

The phantom was also scanned after wrapping it in cooling packs to simulate attenuation and scatter conditions comparable to those in an obese patient.

Following a low-dose CT used for attenuation correction of the subsequent PET scan, PET data were acquired in list mode over a single bed position, covering an axial FoV of 26.3 cm.

The reconstructed imaging time was determined according to the recommendations in the German Guideline for ^{18}F -FDG PET/CT in oncology and the NEMA NU 2-2018 protocol (injection of 5.0 kBq/mL; imaging 60 min p.i.; acquisition duration of 7.8 min for a 26.3 cm FoV). The reconstructed imaging time of the ^{68}Ga - and ^{64}Cu -measurements, respectively, were corrected for the lower decay probability compared to ^{18}F . NEMA PET Body phantom scans were reconstructed in the same manner as the Jaszczak measurements.

Image Analysis

Spatial resolution was evaluated according to (10). Briefly, it was determined based on the analysis of radial activity profiles of the homogeneously filled phantom spheres and assessment of the Full Width at Half Maximum (FWHM) of the Point Spread Function in the reconstructed images. Mean and standard deviation of the FWHM of all six spheres were compared between nuclide measurements.

Quantitative image quality was evaluated using the software Rover (version 3.0.60h, ABX, Radeberg, Germany). Three uniform background regions of interest (ROIs) of at least 61 ml volume were delimited. Spheres were segmented using a 50% background corrected threshold according to (11). For each ROI, mean, maximal and peak Recovery Coefficient (RC_{mean} , RC_{max} and RC_{peak}) were determined as the ratio of the measured mean/maximum/peak SUV of the ROI and the actual activity concentration in the sphere at the timepoint of imaging determined using an activimeter. Mean and standard deviations of the RC values of all six spheres were compared.

Image noise, called percent background variability in NEMA NU 2-2018 protocol, was calculated as Coefficient of Variation within each of the three background ROIs (CoV_{BG}). Mean values of all three ROIs were compared between PET images of different nuclides.

The contrast between each sphere and the background (Contrast Recovery Coefficient (CRC)) was calculated according to NEMA NU 2-2018 protocol. Mean and standard deviations of the percent contrast of all spheres were compared between PET images.

The Contrast-Noise-Ratio (CNR) was calculated as the difference in the SUV_{mean} between each sphere and the background, divided by the standard deviation of the activity concentration in the background compartment. Mean and standard deviations of the CNRs of all spheres were compared between PET images.

According to the NEMA NU 2-2018 protocol, the relative count error in the lung insert was determined as the ratio of the average number of counts in the lung insert of the phantom not filled with radioactivity, relative to the averaged number of counts within the three ROIs placed in the activity-filled phantom background

Impact of Reconstruction Method

Spatial resolution and image quality of the dataset of the NEMA PET Body phantom filled with ^{18}F -FDG with a sphere-to-background activity concentration ratio of 8:1 and normal weight setup were compared quantitatively between different reconstruction parameters applied on the same PET/CT dataset. Based on the reconstruction parameters used by default in our clinical routine for ^{18}F -FDG (OSEM+PSF with 6i5s, ToF, 440 x 440 matrix; allpass), the individual impact of the following parameters on resolution and image quality was investigated: reconstruction algorithm (6i5s/4i5s; with/without application of PSF; with/without application of ToF); matrix size (440 x 440 pixel/220 x 220 pixel); post-filtering (allpass compared to post-filtering with a Gaussian filter (3 mm as well as 5 mm FWHM)).

Results

Analysis of Jaszczak Phantom Measurement for Qualitative Evaluation of Image Resolution

Having adjusted the reconstruction time to the radionuclide-specific half-life, positron fraction (Table 1) and to the activity concentration in the phantom at the timepoint of imaging (Table 2), the total number of true events detected by the PET/CT scanner was similar in ^{18}F -FDG (86.570.998 counts), ^{68}Ga -HCl (81.659.978 counts) and ^{64}Cu -HCl measurements (85.815.118 counts), respectively.

Figure 1 compares the resolution of PET images of the Jaszczak phantom filled with ^{18}F -FDG, ^{68}Ga -HCl and ^{64}Cu -HCl, respectively. The minimum resolvable rods were those separated by 4.8 mm for ^{18}F and ^{64}Cu (smallest rods), respectively, and 6.4 mm for ^{68}Ga measurements (second smallest rods). The smallest of the six cold spheres featuring a diameter of 9.5 mm was clearly recognizable in PET images of all three nuclides.

Analysis of NEMA PET Body Phantom Measurement for Quantitative Evaluation of Spatial Resolution

The number of true counts detected by the PET/CT scanner was similar for scans of the NEMA PET Body phantom filled with the three different nuclides (Table 2). Wrapping the phantom in cooling packs to simulate attenuation and scatter conditions similar to those in an obese patient reduced the number of detected true events by 36.1% (^{68}Ga , 8:1 contrast ratio) to 38.4% (^{68}Ga , 4:1 contrast ratio) (Table 2).

When comparing scans of the NEMA PET Body phantom at similar sphere-to-background contrast ratios and weight setup, spatial resolution was comparable between ^{18}F and ^{64}Cu measurements, but worse in the respective ^{68}Ga measurement (Table 3). For each nuclide, the scan of the phantom mimicking an obese weight setup featured a slightly worse resolution compared to the scan of the phantom not wrapped with cooling packs. Resolution was slightly better in the PET image of phantom filled with a

sphere-to-background activity concentration ratio of 8:1 compared to 4:1, especially in $^{68}\text{Ga-HCl}$ PET/CT images.

Table 3
Spatial resolution (FWHM) in mm determined using the NEMA PET Body phantom.

	4:1 contrast; normal weight setup	4:1 contrast; obese setup	8:1 contrast; normal weight setup	8:1 contrast; obese setup
$^{18}\text{F-FDG}$	4.55 ± 0.18	4.83 ± 0.32	4.10 ± 0.21	4.21 ± 0.24
$^{68}\text{Ga-HCl}$	5.35 ± 0.19	5.35 ± 0.33	4.83 ± 0.16	4.87 ± 0.24
$^{64}\text{Cu-HCl}$	4.35 ± 0.20	4.55 ± 0.19	4.17 ± 0.30	4.30 ± 0.20
Legend Table 3: <i>Spatial resolution is represented by mean and standard deviation of the Full Width at Half Maximum (FWHM) of all six spheres (in mm) of the NEMA PET Body phantom filled with $^{18}\text{F-FDG}$, $^{68}\text{Ga-HCl}$ and $^{64}\text{Cu-HCl}$, respectively, at sphere-to-background activity concentration ratios of 4:1 and 8:1, respectively, and with applying cooling packs around the phantom (obese setup) or without (normal weight setup).</i>				

Quantitative Evaluation of Image Quality

Representative for all NEMA PET Body phantom measurements, figure 2 compares RC_{mean} , RC_{max} , RC_{peak} , CRC and CNR of all spheres of different sizes between $^{18}\text{F-FDG}$, $^{68}\text{Ga-HCl}$ and $^{64}\text{Cu-HCl}$ NEMA PET Body phantom measurements at a sphere-to-background activity concentration ratio of 8:1 and without the simulation of additional attenuation and scattering (obese setup). Mean values are compared between all NEMA PET Body phantom measurements in Attachment - Table 1A.

The mean activity concentrations recovered from the PET/CT images were comparable with the true activity concentrations in all measurements of the NEMA PET Body Phantom, as indicated by $\text{RC}_{\text{mean}} \approx 1$ for measurements independent of nuclide, contrast ratio, weight setup or sphere size.

RC_{mean} and RC_{max} values of the smaller spheres were slightly lower in $^{68}\text{Ga-HCl}$ compared to $^{18}\text{F-FDG}$ and $^{64}\text{Cu-HCl}$ measurements, respectively, while parameters were comparable between $^{18}\text{F-FDG}$ and $^{64}\text{Cu-HCl}$ measurements. The maximal activity concentrations recovered from the PET/CT images were much higher than the true activity concentration in measurements of all nuclides, with lowest RC_{max} values in $^{68}\text{Ga-HCl}$ measurements (1.22 ± 0.04) and highest RC_{max} in $^{64}\text{Cu-HCl}$ measurements (1.51 ± 0.06). In $^{64}\text{Cu-HCl}$ and $^{18}\text{F-FDG}$, but not in $^{68}\text{Ga-HCl}$ measurements, the smallest sphere of 10 mm in diameter featured higher RC_{max} values than the remaining spheres.

For each nuclide, the percent contrast was comparable between different phantom setups and independent of the weight setup and sphere-to-background activity concentration ratio. The CRC was

comparable between ^{18}F -FDG and ^{64}Cu -HCl measurements, but lower in ^{68}Ga -HCl measurements (8:1 sphere-to-background activity concentration ratio and normal weight setup: ^{18}F -FDG: $96.46\% \pm 4.07\%$; ^{64}Cu -HCl: $103.90\% \pm 3.32\%$; ^{68}Ga -HCl: $83.30\% \pm 5.75\%$) (Attachment, Table 1). At both contrast ratios and weight setups of the NEMA PET Body phantom, CNR was lower in ^{68}Ga -HCl compared to ^{64}Cu -HCl and ^{18}F -FDG measurements, respectively.

Image noise was similar for all nuclides when comparing PET images of the NEMA PET Body phantom at the same setup (weight setup & sphere-to-background activity concentration ratio). Image noise was lower in normal weight setup compared to specific obese setup.

For both sphere-to-background activity concentrations, the relative count error in the lung insert was higher for ^{68}Ga -HCl (4:1: 10.72% ; 8:1: 12.62%) compared to ^{18}F -FDG (4:1: 7.23% ; 8:1: 7.75%) and ^{64}Cu -HCl (8:1: 7.40% ; 4:1: 7.29%), respectively.

Quantitative Evaluation of Impact of Reconstruction Method

Spatial resolution was best when standard reconstruction parameters were applied ($4.10 \text{ mm} \pm 0.21 \text{ mm}$). Resolution was worse when ToF measurements were not performed ($5.77 \text{ mm} \pm 0.59 \text{ mm}$) or when data was post-filtered with a Gaussian filter (3 mm FWHM: $4.89 \text{ mm} \pm 0.18 \text{ mm}$; 5 mm FWHM: $6.22 \text{ mm} \pm 0.18 \text{ mm}$). When PSF or ToF was not applied or data was post-filtered, RC_{mean} , RC_{max} and CRC were not comparable between spheres of different sizes and especially the smaller spheres were not fully recovered (Figure 3). The influence of the ToF measurement was particularly noticeable in the recovery of the smallest sphere of 10 mm in diameter. Differences in RC, CRC and CNR values between the standard and modified reconstruction procedure were greatest when a Gaussian filter with 5 mm FWHM was applied. In comparison, a lower iteration number or a smaller matrix size did not affect image quality (Figure 3).

A reconstruction of the data without resolution recovery by PSF increased image noise substantially (OSEM+PSF: 9.7% ; OSEM: 21.6%), while post-filtering of the data with a Gaussian filter reduced image noise (allpass: 9.7% ; 3 mm FWHM: 6.6% ; 5 mm FWHM: 4.2%). Similarly, CNRs were much lower in OSEM reconstruction (35.56 ± 2.67) compared to the OSEM + PSF reconstruction (86.55 ± 3.66) and much higher when post-filtering with a Gaussian filter and 5 mm FWHM was applied (155.98 ± 21.90) (Figure 3).

Discussion

The main finding of this study is that image quality of PET scans of a clinical, digital PET/CT scanner (especially spatial resolution, recovery coefficients and image noise) is strongly affected by the positron energy of the used PET isotope, by reconstruction specific parameters (mainly post-filtering, PSF reconstruction and for small lesions ToF measurements) and by attenuation.

Qualitative and Quantitative Evaluation of Image Resolution

Both our qualitative analyses of the Jaszczak phantom and the quantitative determination of spatial resolution based on measurements of the NEMA PET Body phantom revealed, that spatial resolution is worse in ^{68}Ga compared to both, ^{18}F and ^{64}Cu measurements. Consistently, Sanchez-Crespo et al. and Ryu et al. found worse spatial resolution in ^{68}Ga compared to ^{18}F measurements (12, 13). However, in contrast to the study performed by Sanchez-Crespo (which used the same activity concentration and acquisition time for ^{18}F and ^{68}Ga measurements), in this investigation count rates were comparable between the nuclide measurements. The fact that we can still see differences implies that the higher endpoint energy of positrons originating from the decay of ^{68}Ga and an associated increase in positron range compared to the other nuclides (mean range in water: ^{68}Ga : 3.5 mm; ^{18}F : 0.6 mm; ^{64}Cu : 0.7 mm; (14)), worsens spatial resolution in clinical, digital PET/CT scans. In comparison to $^{68}\text{Ga}\text{-HCl}$, image resolution was comparable between $^{64}\text{Cu}\text{-HCl}$ and $^{18}\text{F}\text{-FDG}$ PET/CT images of the Jaszczak phantom as the positrons arising from the decay of both nuclides feature comparable endpoint energies.

Quantitative Evaluation of Image Quality

The similar number of true events detected by the PET/CT scanner in the measurements of the NEMA PET Body phantom filled with the different nuclides at normal or obese weight setup, respectively (Table 2), indicates that the adjustment of the analyzed recording time accurately compensated for nuclide-specific differences in positron yield and half-life.

It was found, that for objects of ≥ 10 mm in diameter, the mean activity concentration was accurately recovered in $^{18}\text{F}\text{-FDG}$, $^{68}\text{Ga}\text{-HCl}$ and $^{64}\text{Cu}\text{-HCl}$ measurements, giving a $\text{RC}_{\text{mean}} \approx 1$. In comparison, both Sanchez-Crespo et al. (12) and Ryu et al. (13) found in their studies that the scanned object should be at least 20 mm in diameter in both, $^{18}\text{F}\text{-FDG}$ and $^{68}\text{Ga}\text{-HCl}$ images of a clinical PET/CT scanner, in order to accurately recover the true mean activity concentration. The different findings are most likely due to the use of the latest technology PET/CT scanner in this study. Here, a ToF-enabled PET/CT scanner was used, which has shown to exhibit less size-based partial-volume bias than non-time-of-flight scanners (15). This might explain why we found similar differences in RC_{mean} between spheres of different size compared to (12) and (16).

The PSF reconstruction used in this study leads not only to an improved sharpness of hot spheres and higher spatial resolution, but also to an artificial edge overemphasis, which is called the Gibbs artifact (16, 17). This artificial increase in the activity concentration, which occurs especially at the edge of lesions, is illustrated in the radial profiles depicted in Figure 4. This overestimation of the activity concentration is non-linear and increases with decreasing lesion size (Figure 4) (16), which is associated with higher RC_{max} of the smallest spheres of 10 mm in diameter compared to bigger spheres in $^{18}\text{F}\text{-FDG}$ and $^{64}\text{Cu}\text{-HCl}$ measurements. As a consequence of the activity overestimation, the EANM Research Ltd. (EARL) limits are no longer fulfilled (18).

The impact of the Gibbs artifacts might have been comparable between the measurements of the different nuclides since the same reconstruction parameters and methods were used. Nevertheless, in ^{68}Ga -HCl measurements, RC_{mean} and RC_{max} values were lower than for ^{18}F -FDG and ^{64}Cu -HCl, especially for the smallest sphere. This might be due to a higher partial volume effect in ^{68}Ga -HCl measurements (due to the higher positron range), which may outweigh the non-linear effect of artificial edge elevation.

The higher positron range and partial volume effects in ^{68}Ga measurements potentially reduce the contrast between each sphere and background as well as the CNR in ^{68}Ga -HCl compared to ^{64}Cu -HCl and ^{18}F -FDG measurements, respectively. Similarly, Ryu et al. reported higher CRC values in ^{18}F - compared to ^{68}Ga -PET scans. But in contrast to our measurements, CRC decreased with decreasing sphere size in their measurements, potentially due to a reconstruction of the data without resolution recovery by PSF and worse ToF performance (13).

The higher relative count error in the lung insert in the ^{68}Ga -HCl measurements compared to both, ^{18}F -FDG and ^{64}Cu -HCl, is probably a combined effect of the higher range of the positrons (which leads to a stronger penetration of the lung insert) as well as single photon emission and scattered photons arising during the decay of ^{68}Ga but not during the decay of ^{18}F and ^{64}Cu , respectively. In addition, a different scattering correction algorithm was used for the reconstruction of the ^{68}Ga data (^{68}Ga : absolute scatter correction; ^{18}F and ^{64}Cu : relative scatter correction) since the device did not allow any other possibility.

Wrapping the phantom in cooling packs increased scattering and absorption of phantoms and reduced the detected number of true counts, which increased image noise to a similar extent in all nuclide measurements.

Quantitative Evaluation of Reconstruction Method

Reconstruction of image data with a lower number of iterations or a smaller image matrix size had no impact on spatial resolution, image contrast or RC values in our measurements analyzing spheres ≥ 10 mm in diameter.

Consistent with findings by Sunderland and Christian (15), we found that post-filtering had the strongest impact on quantitative parameters describing spatial resolution, image quality and contrast. Similar to (16) and (17), we found that post-filtering reduced image noise as well as Gibbs artifacts associated with PSF reconstruction (which reduced RC_{max} , RC_{mean} and RC_{peak} , respectively, especially of the smaller spheres), but was also associated with a reduction of CRC. The larger the FWHM, the more heterogeneous the recovery and image contrast between spheres of different sizes. In clinical practice, inconsistent recovery coefficients and deviating SUV values between spheres of different sizes could lead to incorrect conclusions if multiple metastases of different sizes are found in PET/CT scans and if diagnosis is based on SUV thresholds.

Except for OSEM without PSF reconstruction, all reconstruction methods resulted in a background noise level $< 15\%$, which is considered as an acceptable noise level as of the EARL procedure (16).

Reconstruction without PSF increased image noise to a non-acceptable level and was associated with a reduction of the CRCs of spheres of different sizes, which in combination greatly reduced CNRs of all spheres substantially.

Consistent with (15), we found that ToF measurements were particularly noticeable for the recovery of small lesions. While all other spheres were recovered well, the sphere of 10 mm in diameter revealed much lower RC_{max} , RC_{mean} , RC_{peak} , and CRC values when ToF measurements were not applied.

We have found that using a different reconstruction method (like no PSF) and/or scanner technology (like no ToF measurement or analog/digital as shown in (19)) can result in large differences in the SUV. This once again underlines, that comparisons of quantitative image data acquired in different imaging centers using different scanners or reconstruction methods are problematic.

Conclusion

In summary, we found that image quality was similar between ^{18}F -FDG and ^{64}Cu -HCl PET/CT images featuring similar maximal endpoint energy and, thus, a similar maximum range of positrons in tissue before annihilation. In comparison, the much higher endpoint energy of positrons arising from the decay of ^{68}Ga reduced image quality (RC, CRC and CNR) and spatial resolution.

In ^{18}F -FDG PET/CT, post-filtering had the strongest impact on spatial resolution and image quality. ToF measurements are especially valuable for the recovery of smallest lesions.

List Of Abbreviations

SUV - Standardized Uptake Value

ToF - Time of Flight

PSF - Point Spread Function

HCl - HydroChloric acid

FoV - Field of View

OSEM - Ordered Subset Expectation Maximization

FWHM - Full Width at Half Maximum

ROI - Region Of Interest

RC - Recovery Coefficient

CoV_{BG} - Coefficient of Variation within the background ROI

CRC - Contrast Recovery Coefficient

CNR - Contrast-Noise-Ratio

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and material

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

Not applicable.

Authors' contributions

A.B., R.F., L.O., J.K. and S.H. contributed to design of the study and discussed the data.

A.B. planned, performed and analyzed the measurement.

A.B. was a major contributor in writing the manuscript.

S.H. is the Senior Author.

All authors discussed the results and implications and commented on the manuscript.

All authors read and approved the final manuscript.

Acknowledgements

Not applicable.

References

1. Kroenke M, Mirzoyan L, Horn T, Peeken JC, Wurzer A, Wester HJ, et al. Matched-Pair Comparison of (68)Ga-PSMA-11 and (18)F-rhPSMA-7 PET/CT in Patients with Primary and Biochemical Recurrence of Prostate Cancer: Frequency of Non-Tumor-Related Uptake and Tumor Positivity. *J Nucl Med*. 2021;62(8):1082-8.
2. Rauscher I, Kronke M, König M, Gafita A, Maurer T, Horn T, et al. Matched-Pair Comparison of (68)Ga-PSMA-11 PET/CT and (18)F-PSMA-1007 PET/CT: Frequency of Pitfalls and Detection Efficacy in Biochemical Recurrence After Radical Prostatectomy. *J Nucl Med*. 2020;61(1):51-7.
3. Hoberuck S, Lock S, Borkowetz A, Sommer U, Winzer R, Zophel K, et al. Intraindividual comparison of [(68) Ga]-Ga-PSMA-11 and [(18)F]-F-PSMA-1007 in prostate cancer patients: a retrospective single-center analysis. *EJNMMI Res*. 2021;11(1):109.
4. İlhan H, Lindner S, Todica A, Cyran CC, Tiling R, Auernhammer CJ, et al. Biodistribution and first clinical results of (18)F-SiFalin-TATE PET: a novel (18)F-labeled somatostatin analog for imaging of neuroendocrine tumors. *Eur J Nucl Med Mol Imaging*. 2020;47(4):870-80.
5. Kotzerke J, van den Hoff J. Quantification: there is more to worry about than good scanner hardware and reliable calibration. *Eur J Nucl Med Mol Imaging*. 2017;44(12):1955-7.
6. Disselhorst JA, Brom M, Laverman P, Slump CH, Boerman OC, Oyen WJ, et al. Image-quality assessment for several positron emitters using the NEMA NU 4-2008 standards in the Siemens Inveon small-animal PET scanner. *J Nucl Med*. 2010;51(4):610-7.
7. Teuho J, Riehakainen L, Honkaniemi A, Moisio O, Han C, Tirri M, et al. Evaluation of image quality with four positron emitters and three preclinical PET/CT systems. *EJNMMI Res*. 2020;10(1):155.
8. Arnfield EG, Thomas PA, Roberts MJ, Pelecanos AM, Ramsay SC, Lin CY, et al. Clinical insignificance of [(18)F]PSMA-1007 avid non-specific bone lesions: a retrospective evaluation. *Eur J Nucl Med Mol Imaging*. 2021.
9. Conti M, Eriksson L. Physics of pure and non-pure positron emitters for PET: a review and a discussion. *EJNMMI Phys*. 2016;3(1):8.
10. Hofheinz F, Dittrich S, Potzsch C, Hoff J. Effects of cold sphere walls in PET phantom measurements on the volume reproducing threshold. *Phys Med Biol*. 2010;55(4):1099-113.
11. Boellaard R, O'Doherty MJ, Weber WA, Mottaghy FM, Lonsdale MN, Stroobants SG, et al. FDG PET and PET/CT: EANM procedure guidelines for tumour PET imaging: version 1.0. *Eur J Nucl Med Mol Imaging*. 2010;37(1):181-200.
12. Sanchez-Crespo A. Comparison of Gallium-68 and Fluorine-18 imaging characteristics in positron emission tomography. *Appl Radiat Isot*. 2013;76:55-62.
13. Ryu H, Meikle SR, Willowson KP, Eslick EM, Bailey DL. Performance evaluation of quantitative SPECT/CT using NEMA NU 2 PET methodology. *Phys Med Biol*. 2019;64(14):145017.
14. Pagani M, Stone-Elander S, Larsson SA. Alternative positron emission tomography with non-conventional positron emitters: effects of their physical properties on image quality and potential clinical applications. *Eur J Nucl Med*. 1997;24(10):1301-27.

15. Sunderland JJ, Christian PE. Quantitative PET/CT scanner performance characterization based upon the society of nuclear medicine and molecular imaging clinical trials network oncology clinical simulator phantom. J Nucl Med. 2015;56(1):145-52.
16. Kaalep A, Huisman M, Sera T, Vugts D, Boellaard R, Earl, et al. Feasibility of PET/CT system performance harmonisation for quantitative multicentre (89)Zr studies. EJNMMI Phys. 2018;5(1):26.
17. Lasnon C, Desmonts C, Quak E, Gervais R, Do P, Dubos-Arvis C, et al. Harmonizing SUVs in multicentre trials when using different generation PET systems: prospective validation in non-small cell lung cancer patients. Eur J Nucl Med Mol Imaging. 2013;40(7):985-96.
18. Kaalep A, Burggraaff CN, Pieplenbosch S, Verwer EE, Sera T, Zijlstra J, et al. Quantitative implications of the updated EARL 2019 PET-CT performance standards. EJNMMI Phys. 2019;6(1):28.
19. Grunig H, Maurer A, Thali Y, Kovacs Z, Strobel K, Burger IA, et al. Focal unspecific bone uptake on [(18)F]-PSMA-1007 PET: a multicenter retrospective evaluation of the distribution, frequency, and quantitative parameters of a potential pitfall in prostate cancer imaging. Eur J Nucl Med Mol Imaging. 2021;48(13):4483-94.

Figures

Figure 1

Image quality of the Jaszczak phantom filled with ^{18}F -FDG (left), ^{68}Ga -HCl (middle) and ^{64}Cu -HCl (right).

Legend Figure 1: Images were acquired and reconstructed using the same scanner and reconstruction methods.

Figure 2

Comparison of quantitative image quality of the NEMA PET Body phantom between ^{18}F -FDG, ^{68}Ga -HCl and ^{64}Cu -HCl.

Legend Figure 2: Quantitative image quality specified as mean, maximal and peak Recovery Coefficient (RC_{mean} , RC_{max} and RC_{peak}), percent contrast between each sphere and the background (Contrast Recovery Coefficient (CRC)) and Contrast-Noise-Ratio (CNR) for each of the six spheres of the NEMA PET Body phantom filled with ^{18}F -FDG, ^{68}Ga -HCl and ^{64}Cu -HCl, respectively, at a sphere-to-background activity concentration ratio of 8:1 without the simulation of an obese patient (normal weight setup).

Figure 3

Impact of different reconstruction methods on quantitative image quality.

Legend Figure 3: Impact of different reconstruction methods on quantitative image quality specified as mean, maximal and peak Recovery Coefficient (RC_{mean} , RC_{max} and RC_{peak}), percent background variability (CoV_{BG}), percent contrast between each sphere and the background (Contrast Recovery Coefficient (CRC)) and Contrast-Noise-Ratio (CNR) for each of the six spheres of the NEMA PET Body phantom filled with ^{18}F -FDG at a sphere-to-background activity concentration ratio of 8:1 without the simulation of an obese patient (normal weight setup). The reconstruction parameters used by default in our clinical routine for ^{18}F -FDG (referred to as Standard Parameter) are the following: Ordered Subset Expectation Maximization (OSEM) and Point Spread Function (PSF) with 6 iterations and 5 subsets (6i5s), Time of Flight measurements (ToF), 440 x 440 matrix; allpass. Based on the Standard Parameters, the individual impact of the following reconstruction parameters were investigated: with/without application of PSF (no PSF); with/without application of ToF (no ToF); 6i5s/4i5s, 440 x 440 matrix size/220 x 220 pixel (220 Matrix) and post-filtering (allpass compared to post-filtering with a Gaussian filter (Gauss 3 mm FWHM as well as Gauss 5 mm FWHM)).

Figure 4

Radial profile of the normalized activity concentration of spheres filled with ^{18}F -FDG, ^{68}Ga -HCl or ^{64}Cu -HCl.

Legend Figure 4: Radial profile of the ratio of measured and true activity concentration of the smallest sphere (upper row; radius: 5 mm) and largest sphere (lower row; radius: 18.5 mm) of the NEMA PET Body phantom filled with ^{18}F -FDG, ^{68}Ga -HCl or ^{64}Cu -HCl (from left to right) at a sphere-to-background activity concentration ratio of 8:1 without the simulation of an obese patient (normal weight setup). The solid line represents the least-square fit of the convolution of the Point Spread Function and the object geometry, analyzed to yield the FWHM. To guide the eye, the dashed lines represent a mean ratio of measured and actual activity concentration of one.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [SupplementaryMaterialBraunelImageQualityDec2021.docx](#)