Research Square

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The Impact of Different Reconstruction Algorithms on Quantitative Parameters and Image Quality in Ga-68 DOTATATE PET/CT Imaging

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Abstract

Background

Herein, we aimed to evaluate the effects of different Bayesian penalized-likelihood (BPL) reconstruction penalization factors on semi-quantitative parameters in Ga-68 DOTATATE PET/CT compared with conventional ordered subsets expectation maximization (OSEM), with particular emphasis on lesion size-dependent effects.

Methods

A total of 102 Ga-68 DOTATATE-avid lesions from 45 prospectively enrolled patients were evaluated using BPL and OSEM algorithms on Ga-68 DOTATATE PET/CT. Images were reconstructed from identical acquisition datasets using conventional OSEM and Q.Clear with β values of 600, 800, and 1000. Lesion SUVmax, SUVmean, tumor-to-liver ratio (TLR), liver signal-to-noise ratio (SNR), and contrast-to-noise ratio (CNR) were compared across reconstruction methods. Statistical analyses accounted for within-patient clustering and multiple comparisons. A linear mixed-effects model was used to investigate the interaction between reconstruction method and lesion diameter.

Results

Compared with OSEM, Q.Clear β600 significantly increased lesion SUVmax (11.08 vs. 9.13; adjusted $p = 0.0012$), SUVmean (7.51 vs. 5.73; $p = 0.0296$), TLR (1.69 vs. 1.42; $p = 0.0036$), and CNR (7.28 vs. 3.66; $p < 0.001$). β800 also significantly improved lesion SUVmax, SUVmean, and CNR, whereas β1000 showed no significant improvement in these parameters compared with OSEM. Liver SNR increased with higher β values, reaching its highest mean value at β1000 (13.54 vs. 10.66 for OSEM; adjusted $p < 0.01$). A significant interaction was observed between reconstruction method and lesion diameter ($p = 0.0039$). With β600, the median SUVmax increase relative to OSEM was 27.3% for lesions < 10 mm, 15.8% for lesions 10–<20 mm, and 10.1% for lesions ≥ 20 mm.

Conclusions

Q.Clear reconstruction significantly affects semi-quantitative measurements in Ga-68 DOTATATE PET/CT, with effects dependent on penalization strength and lesion size. β600 provided greater lesion uptake and contrast measurements, particularly in smaller lesions, whereas higher β values improved background noise suppression. These findings emphasize the importance of balancing quantitative lesion contrast and image noise and maintaining consistent reconstruction protocols for longitudinal PET/CT assessment.

Background

Ga-68 DOTATATE positron emission tomography/computed tomography (PET/CT) has become an essential imaging modality for patients with neuroendocrine tumors, providing valuable information for tumor staging, assessment of somatostatin receptor expression, and selection of appropriate therapeutic strategies. Because treatment decisions and response assessment increasingly rely on quantitative imaging biomarkers, accurate and reproducible lesion-specific measurements are of growing clinical importance [1]. However, despite the widespread clinical use of Ga-68 DOTATATE PET/CT, a fully standardized quantitative approach for treatment response evaluation has not yet been established. Quantitative PET measurements may be influenced by multiple technical factors, including administered radiotracer activity, uptake time, bed position acquisition time, and image reconstruction methodology [2].

Image reconstruction represents one of the major determinants of both image quality and quantitative accuracy in PET imaging. For many years, ordered subsets expectation maximization (OSEM) has served as the conventional iterative reconstruction algorithm in routine clinical practice. More recently, Bayesian penalized likelihood (BPL) reconstruction techniques, including Q.Clear (General Electric Healthcare, Milwaukee, USA), have gained widespread acceptance owing to their improved quantitative performance [3]. This approach enables full convergence while suppressing image noise, resulting in improved lesion-to-background contrast, enhanced quantitative accuracy, and high-quality PET images that may also facilitate reduced administered radiotracer activity [4].

In Q.Clear reconstruction, the degree of penalization is governed by the regularization parameter β, which modulates the trade-off between image noise suppression and preservation of spatial resolution. Lower β values generally produce higher lesion contrast at the expense of increased image noise, whereas higher β values reduce image noise but may compromise lesion conspicuity. Consequently, selecting an appropriate β value is critical for optimizing both image quality and quantitative accuracy [5].

Previous studies have demonstrated that Q.Clear improves lesion detectability and semi-quantitative measurements, particularly for small lesions, compared with conventional OSEM reconstruction in 18F-FDG PET/CT imaging [6–9]. Nevertheless, the optimal β value remains controversial, as recommended settings vary considerably among studies depending on scanner characteristics, radiotracer, and clinical application. Furthermore, while the effects of Q.Clear have been extensively investigated in F-18 FDG PET/CT, evidence regarding its influence on quantitative parameters in Ga-68 DOTATATE PET/CT remains scarce.

Therefore, the present study aimed to evaluate the effects of conventional OSEM reconstruction and Q.Clear reconstruction using different β values on semi-quantitative measurements in Ga-68 DOTATATE PET/CT imaging.

Methods

Study design and patient selection

This prospective observational study consecutively enrolled patients who underwent Ga-68 DOTATATE PET/CT imaging between January 2026 and August 2026. Patients were eligible for inclusion if at least one lesion demonstrating pathological Ga-68 DOTATATE uptake was identified on PET/CT. Overall, 45 patients with a total of 102 lesions met the inclusion criteria and were included in the final analysis.

Ga-68 DOTATATE PET/CT acquisition

All Ga-68 DOTATATE PET/CT scans were conducted using a hybrid PET/CT scanner (GE Discovery IQ 5-Ring; GE Healthcare, Milwaukee, WI) in the Nuclear Medicine Department. Ga-68 DOTATATE was administered intravenously, with a mean administered activity of 172.8 ± 50.4 MBq (range, 81.4–277.5 MBq). PET acquisition commenced at a mean of 58.9 ± 10.7 min (range, 43–86 min) following radiotracer injection. Image acquisition began with a low-dose CT scan covering the region from the skull base to the mid-thigh, performed using a 16-slice multidetector CT system. The CT acquisition settings included a tube current of 80 mA, tube voltage of 140 kV, table advancement of 27 mm per rotation, and reconstructed slice thickness of 3 mm. Subsequently, PET data were acquired over the corresponding anatomical region in three-dimensional mode, with an acquisition duration of 3 minutes per bed position, requiring six to eight bed positions per patient.

Image reconstruction and Quantitative analysis

PET list-mode data were reconstructed using both the conventional three-dimensional ordered subset expectation maximization (3D OSEM) algorithm and the Bayesian penalized likelihood (BPL) reconstruction algorithm (Q.Clear, GE Healthcare). The OSEM images were reconstructed with 3 iterations, 8 subsets, a 6-mm Gaussian post-reconstruction filter, and an acquisition time of 3 min per bed position. BPL reconstructions were generated from the same raw datasets using acquisition times of 3 min per bed position with β values of 600, 800, and 1000. Semi-quantitative image analysis was performed using Advantage Workstation software (GE Healthcare). Three-dimensional volumes of interest (VOIs) were automatically generated around each lesion using a 40% SUVmax threshold, from which lesion SUVmax and SUVmean were obtained. For background assessment, a 3-cm-diameter spherical VOI was placed in a homogeneous, lesion-free region of the right hepatic lobe to measure liver SUVmean and its standard deviation (SD). Tumor-to-liver ratio (TLR), also referred to as the signal-to-background ratio (SBR), was calculated as the ratio of lesion SUVmax to liver SUVmean [10]. Liver signal-to-noise ratio (SNR) was calculated by dividing liver SUVmean by the standard deviation of liver uptake (liver SD) [11]. Contrast-to-noise ratio (CNR) was calculated as the difference between lesion SUVmax and liver SUVmean divided by liver SD [12]. The following semi-quantitative parameters were recorded for each reconstruction: lesion SUVmax, lesion SUVmean, liver SUVmean, liver SD, TLR (SBR), liver SNR, and CNR.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics (IBM Corp., Armonk, NY, USA). Continuous variables were summarized as mean ± standard deviation (SD) or median and interquartile range (IQR), as appropriate, while categorical variables were expressed as frequencies and percentages. Quantitative lesion parameters, including SUVmax, SUVmean, tumor-to-liver ratio (TLR), and contrast-to-noise ratio (CNR), were compared across conventional OSEM and Q.Clear reconstructions with penalization factors (β) of 600, 800, and 1000. Because multiple lesions could originate from the same patient and each lesion was evaluated using all four reconstruction methods, within-patient clustering was accounted for using cluster-robust standard errors. Pairwise differences between reconstruction methods were assessed using patient-cluster-adjusted comparisons, with Holm correction applied to control for multiple testing. Liver background parameters, including SUVmean, standard deviation (SD), and signal-to-noise ratio (SNR), were analyzed at the patient level, using one set of liver measurements per patient for each reconstruction method. Overall differences across the four reconstruction methods were evaluated using the Friedman test. When appropriate, post hoc pairwise comparisons were performed using the Wilcoxon signed-rank test, with Holm adjustment for multiple comparisons. To investigate whether the effect of reconstruction method on lesion SUVmax varied according to lesion size, a linear mixed-effects model was fitted using log-transformed SUVmax as the dependent variable. Reconstruction method, lesion diameter (mm), and their interaction were included as fixed effects. Random intercepts were specified at the patient and lesion-within-patient levels to account for multiple lesions per patient and repeated measurements of each lesion across reconstruction methods. OSEM was used as the reference reconstruction. Models with and without the interaction term were fitted using maximum likelihood estimation and compared using a likelihood-ratio test. Regression coefficients, 95% confidence intervals, and corresponding p-values were calculated. Lesion size categories (<10 mm, 10 to <20 mm, and ≥20 mm) were additionally used for descriptive subgroup analyses. A two-sided p-value <0.05 was considered statistically significant. Adjusted p-values were reported for multiple pairwise comparisons.

Results

Patient and Lesion Characteristics

A total of 45 patients (24 men and 21 women) were included in the study. The mean age was 55.3 ± 13.7 years (range, 18–80 years). The mean body mass index (BMI) was 27.6 ± 4.6 kg/m² (range, 20.9–42.6 kg/m²). The most common primary tumor sites were the pancreas (n=9, 20.0%) and stomach (n=9, 20.0%), followed by the thyroid (n=7, 15.6%), lung (n=6, 13.3%), and small intestine (n=4, 8.9%). Other primary tumor sites and tumors of unknown origin accounted for the remaining cases. The mean administered radiotracer activity was 173.9 ± 51.8 MBq, and the mean uptake time was 58.9 ± 10.7 minutes.

The mean lesion diameter was 17.0 ± 10.4 mm (range, 5–50 mm). Of the 102 lesions, 31 (30.4%) were smaller than 10 mm, 31 (30.4%) measured 10 to less than 20 mm, and 40 (39.2%) measured 20 mm or greater. Detailed patient and lesion characteristics are presented in Table 1.

Table 1: Patient and lesion characteristics

Characteristics	Values
Patient characteristics (n = 45)	
Age (years), mean ± SD	55.3 ± 13.7
Age range (years)	18–80
Sex, n (%)	
Male	24 (53.3%)
Female	21 (46.7%)
Height (cm), mean ± SD	165.9 ± 9.7
Weight (kg), mean ± SD	75.9 ± 13.2
BMI (kg/m²), mean ± SD	27.6 ± 4.6
BMI ≥25 kg/m², n (%)	29 (64.4%)
BMI ≥30 kg/m², n (%)	13 (28.9%)
Primary tumor type, n (%)	
Pancreatic NET	9 (20.0%)
Gastric NET	9 (20.0%)
Medullary Thyroid Cancer	7 (15.6%)
Lung carcinoid	6 (13.3%)
Small bowel NET	4 (8.9%)
Unknown origin	3 (6.7%)
Pheochromocytoma	2 (4.4%)
Paraganglioma	2 (4.4%)
Colon	1 (2.2%)
Gastrinoma	1 (2.2%)
Liver	1 (2.2%)
PET/CT acquisition characteristics	
Administered activity (MBq), mean ± SD	172.8 ± 50.4
Uptake time (min), mean ± SD	58.9 ± 10.7
Lesion characteristics (n = 102)	
Total number of lesions	102

Lesions per patient, mean	2.27
Lesion diameter (mm), mean ± SD	17.0 ± 10.4
Lesion diameter, median (mm)	15.0
Lesion diameter range (mm)	5–50
Lesion size categories, n (%)	
<10 mm	31 (30.4%)
10–<20 mm	31 (30.4%)
≥20 mm	40 (39.2%)

Values are presented as mean ± standard deviation (SD), median, range, or number (percentage), as appropriate. BMI, body mass index; NET, neuroendocrine tumor; PET/CT, positron emission tomography/computed tomography.

Comparison of Lesion Quantitative Parameters

Lesion SUVmax differed across reconstruction methods, with mean values of 9.13 ± 11.80 for OSEM, 11.08 ± 14.00 for β600, 10.13 ± 12.99 for β800, and 9.90 ± 12.63 for β1000. Compared with OSEM, β600 demonstrated a significantly higher mean SUVmax (mean difference, 1.95; Holm-adjusted $p = 0.0012$), as did β800 (mean difference, 1.00; adjusted $p = 0.0184$). The difference between β1000 and OSEM was not statistically significant (adjusted $p = 0.370$). β600 also yielded a significantly higher SUVmax than β800 (adjusted $p < 0.001$), whereas the differences between β600 and β1000 and between β800 and β1000 were not statistically significant after adjustment.

A similar pattern was observed for lesion SUVmean. Mean values were 5.73 ± 7.51 with OSEM, 7.51 ± 10.83 with β600, 6.52 ± 8.43 with β800, and 6.30 ± 8.12 with β1000. Both β600 and β800 produced significantly higher SUVmean values than OSEM (adjusted $p = 0.0296$ and $p = 0.0085$, respectively), whereas β1000 did not differ significantly from OSEM.

The mean tumor-to-liver SUV ratio (TLR) was 1.42 ± 1.92 for OSEM, 1.69 ± 2.19 for β600, 1.55 ± 2.07 for β800, and 1.51 ± 2.01 for β1000. Compared with OSEM, a statistically significant increase in TLR was observed with β600 (adjusted $p = 0.0036$). β600 also yielded a significantly higher TLR than β800 (adjusted $p < 0.001$). Other pairwise differences did not remain statistically significant after correction for multiple comparisons.

Background Noise and Liver Signal-to-Noise Ratio

Liver SUVmean remained relatively stable across reconstruction methods, with mean values of 8.25 for OSEM, 8.28 for β600, 8.32 for β800, and 8.32 for β1000. Nevertheless, a statistically significant overall difference was detected (Friedman test, $p = 0.002$).

Correspondingly, mean liver signal-to-noise ratio (SNR) increased from 10.66 ± 2.48 with OSEM to 11.53 ± 2.90 with β600, 12.82 ± 3.71 with β800, and 13.54 ± 4.67 with β1000. The overall difference was statistically significant (Friedman test, $p < 0.001$). All three Q.Clear reconstructions demonstrated significantly higher liver SNR than OSEM after Holm correction (all adjusted $p < 0.01$). Both β800 and β1000 also yielded significantly higher SNR than β600 (both adjusted $p < 0.001$). Although β1000 produced the highest mean liver SNR, its difference from β800 was not statistically significant (adjusted $p = 0.055$).

Contrast-to-Noise Ratio

The mean contrast-to-noise ratio (CNR) was 3.66 ± 16.67 with OSEM, 7.28 ± 22.42 with β600, 5.86 ± 22.48 with β800, and 4.88 ± 22.16 with β1000. Compared with OSEM, both β600 and β800 demonstrated significantly higher CNR values (adjusted $p < 0.001$ and $p = 0.0244$, respectively), whereas the difference for β1000 was not statistically significant.

Among the Q.Clear reconstructions, β600 yielded significantly higher CNR than β800 and β1000 (both adjusted $p < 0.001$). CNR was also significantly higher with β800 than with β1000 (adjusted $p = 0.0131$).

Table 2: Quantitative comparison of reconstruction methods

Parameter	OSEM	Q.Clear β600	Q.Clear β800	Q.Clear β1000
Lesion SUVmax	9.13 ± 11.80	11.08 ± 14.00	10.13 ± 12.99	9.90 ± 12.63
Lesion SUVmean	5.73 ± 7.51	7.51 ± 10.83	6.52 ± 8.43	6.30 ± 8.12
TLR	1.42 ± 1.92	1.69 ± 2.19	1.55 ± 2.07	1.51 ± 2.01
Liver SUVmean	8.25	8.28	8.32	8.32
Liver SD	0.843	0.789	0.730	0.736
Liver SNR	10.66 ± 2.48	11.53 ± 2.90	12.82 ± 3.71	13.54 ± 4.67
CNR	3.66 ± 16.67	7.28 ± 22.42	5.86 ± 22.48	4.88 ± 22.16

Data are presented as mean ± standard deviation (SD) or mean, as appropriate.

Influence of Lesion Size on SUVmax

The relative change in lesion SUVmax compared with OSEM varied according to lesion diameter. For β600, the median percentage increase was 27.3% in lesions smaller than 10 mm, 15.8% in lesions

measuring 10 to less than 20 mm, and 10.1% in lesions measuring 20 mm or greater. The corresponding increases for β800 were 11.8%, 5.4%, and 4.1%, respectively.

In exploratory patient-cluster-adjusted regression analysis, increasing lesion diameter was associated with a smaller percentage SUVmax increase relative to OSEM for β600 (regression coefficient, −0.71 percentage points/mm; $p < 0.001$) and β800 (−0.37 percentage points/mm; $p = 0.001$). No statistically significant association was observed for β1000 ($p = 0.260$).

Interaction Between Lesion Size and Reconstruction Method

A linear mixed-effects model was fitted to assess the effects of reconstruction method, lesion diameter, and their interaction on log-transformed SUVmax. The model included random intercepts for patients and lesions nested within patients to account for the hierarchical structure of the data and repeated measurements across reconstruction methods.

A significant overall interaction was observed between reconstruction method and lesion diameter (likelihood-ratio $\chi^2(3) = 13.40$, $p = 0.0039$), indicating that reconstruction-dependent differences in SUVmax varied according to lesion size.

Compared with OSEM, the interaction between lesion diameter and Q.Clear β600 was significant (β = −0.0056 per mm, $p = 0.001$), indicating that the relative SUVmax advantage of β600 decreased with increasing lesion diameter. A weaker interaction was observed for β800 (β = −0.0032 per mm, $p = 0.048$), whereas the interaction for β1000 was not statistically significant ($p = 0.500$).

These findings suggest that the quantitative impact of Q.Clear reconstruction is particularly pronounced in smaller lesions, especially at β600.

Representative Ga-68 DOTATATE PET/CT images illustrating the effects of different reconstruction methods on SUVmax measurements in metastatic lesions of varying sizes are presented in Figure 1.

Maximum-intensity projection (MIP) images are shown in the upper row, followed by axial fused PET/CT images demonstrating metastatic lesions of different sizes. A 10-mm cervical lymph node metastasis (arrow) exhibited SUVmax values of 2.7, 2.5, 2.3, and 2.2, respectively. A 4-cm right superior mediastinal lesion (dashed arrow) showed SUVmax values of 5.7, 5.4, 5.1, and 5.4, respectively. A 5-mm bone metastasis (arrowhead) demonstrated SUVmax values of 2.2, 1.9, 1.6, and 1.5, respectively. A 12-mm hepatic metastasis (thick arrow) exhibited SUVmax values of 16.9, 15.9, 15.2, and 17.9, respectively.

Discussion

In the present prospective study, we evaluated the effects of different Q.Clear penalization factors on semi-quantitative parameters in Ga-68 DOTATATE PET/CT and compared their performance with

conventional OSEM reconstruction. Our findings demonstrated that Q.Clear significantly influenced lesion uptake measurements, lesion-to-background contrast, and background noise, with the magnitude of these effects depending on the selected β value. Among the evaluated reconstruction settings, β600 provided significantly higher lesion SUVmax, SUVmean, tumor-to-liver ratio (TLR), and contrast-to-noise ratio (CNR) values than OSEM, whereas higher β values resulted in greater background noise suppression and improved liver signal-to-noise ratio (SNR). Importantly, reconstruction-dependent changes in SUVmax were significantly influenced by lesion size, with the greatest relative increases observed in smaller lesions. These findings highlight the importance of considering both lesion characteristics and the balance between contrast recovery and noise suppression when selecting reconstruction parameters for Ga-68 DOTATATE PET/CT.

Our findings are consistent with previous investigations demonstrating the quantitative advantages of Bayesian penalized-likelihood reconstruction in Ga-68 DOTATATE PET/CT. Chicheportiche et al. [10] evaluated Q.Clear reconstruction in 30 patients using different penalization factors and acquisition times. At 1.5 min per bed position, Q.Clear β1100 provided a 14% increase in lesion SUVmax, accompanied by improvements of 30% in SNR and 13% in signal-to-background ratio compared with OSEM. Similarly, Temple and Prem [13] reported significantly higher lesion SUVmax values with Q.Clear across the evaluated β values in 25 Ga-68 DOTATATE PET/CT examinations. In our study, both β600 and β800 significantly increased lesion SUVmax and SUVmean compared with OSEM, while β600 also provided a significant improvement in TLR. The higher uptake measurements obtained with Q.Clear may be attributed to improved convergence and contrast recovery compared with conventional OSEM, in which iterations are typically terminated before full convergence to limit noise amplification. However, differences in scanner characteristics, acquisition protocols, and reconstruction settings should be considered when comparing the magnitude of quantitative changes across studies.

The relationship between penalization strength and image quality represents an important consideration in Q.Clear reconstruction. Lower β values generally favor lesion contrast, whereas higher β values provide stronger noise suppression. In our study, β600 yielded the highest mean lesion SUVmax and CNR values, while β1000 provided the highest mean liver SNR. Nevertheless, the difference in liver SNR between β800 and β1000 did not reach statistical significance. Previous studies have reported different preferred β values depending on their evaluation criteria. Temple and Prem [13] identified β800 as the preferred setting for qualitative image quality in Ga-68 DOTATATE PET/CT. Caribé et al. suggested that β750 provided improved performance compared with OSEM [14]. In a small cohort of 13 patients undergoing Ga-68 DOTATOC PET/CT, Lindström et al. reported the lowest noise levels at β values of 400 or higher [15]. In contrast, Zanoni et al. [16] reported that β1600 was visually preferred over lower β values in overweight patients undergoing Ga-68 DOTANOC PET/CT. In a subsequent study by the same research group, Di Franco et al. [17] demonstrated improved overall image quality and small-lesion visualization with β1600 in digital Ga-68 DOTANOC imaging. These apparently different findings may reflect variations in radiotracers, scanner technology, patient characteristics, and the relative importance assigned to lesion contrast and background uniformity. Importantly, visual image quality and quantitative

lesion contrast represent distinct outcomes, and a reconstruction setting that maximizes one parameter may not necessarily optimize the other.

An important methodological consideration in the present study is the calculation of CNR using lesion SUVmax rather than SUVmean, as employed in some previous studies [16]. This approach was selected because SUVmax is widely used in routine oncologic PET reporting and is particularly sensitive to reconstruction-dependent changes in lesion uptake. Furthermore, the use of SUVmax provided consistency with the calculation of TLR, which was also based on lesion SUVmax. In Ga-68 DOTATATE PET/CT, where small lesions and heterogeneous tracer uptake may present challenges for quantitative assessment, SUVmax-based CNR may provide additional information regarding the contrast between the highest-uptake portion of a lesion and the surrounding background. However, SUVmax is also sensitive to image noise, and CNR values calculated using SUVmax are not directly interchangeable with those derived from SUVmean. Therefore, differences in CNR definitions should be considered when comparing reconstruction performance across studies.

A particularly relevant finding of our study was the significant interaction between lesion diameter and reconstruction method. With β600, the median increase in SUVmax relative to OSEM was 27.3% for lesions < 10 mm, 15.8% for lesions 10–20 mm, and 10.1% for lesions ≥ 20 mm. A similar, although less pronounced, pattern was observed with β800. Furthermore, the linear mixed-effects model demonstrated a significant overall interaction between reconstruction method and lesion diameter ($p = 0.0039$), with the relative SUVmax advantage of β600 decreasing as lesion size increased. These findings are consistent with previous evidence suggesting that reconstruction-dependent quantitative differences are more pronounced in smaller lesions. Kurita et al. reported that the use of BPL reconstruction enhanced the detectability of small (< 10 mm), visually subtle malignant pulmonary lesions, contributing to improved diagnostic performance in FDG PET/CT imaging [18]. You et al. [19] evaluated 125 Ga-68 DOTATATE lesions and demonstrated that point-spread function reconstruction increased SUVmax, with greater differences observed in lesions smaller than 2 cm. Similarly, Liu et al. [20] reported that improvements in SNR and tumor-to-background ratio with total variation regularized expectation maximization reconstruction were greater in smaller lesions. Although these studies employed reconstruction methods different from Q.Clear, their findings support the size-dependent nature of reconstruction effects. Our study adds to this evidence by formally evaluating the interaction between lesion diameter and Q.Clear reconstruction while accounting for repeated lesion measurements and clustering within patients.

The greater relative SUVmax increase observed in smaller lesions may be partly explained by differences in contrast recovery and partial-volume effects. Limited spatial resolution causes activity underestimation in small lesions, making their quantitative measurements particularly sensitive to reconstruction methodology. The physical properties of Ga-68, including its relatively long positron range, may further contribute to spatial resolution limitations. Gavriilidis et al. [21] demonstrated that incorporating Ga-68 positron range correction into iterative PET reconstruction improved recovery coefficients and spatial resolution under comparable noise conditions. Although positron range

correction was not investigated in our study, these findings illustrate the importance of reconstruction-related physical factors in Ga-68 PET quantification. The size-dependent changes observed in our analysis suggest that reconstruction settings should be carefully considered when interpreting quantitative measurements in small somatostatin receptor-positive lesions. Nevertheless, the greater SUVmax recovery observed in smaller lesions should not necessarily be interpreted as improved quantitative accuracy, as no independent reference standard was available to determine the true activity concentration.

These findings may have important implications for longitudinal Ga-68 DOTATATE PET/CT assessment. Differences in reconstruction methodology may produce changes in SUV measurements that are unrelated to biological alterations in tumor activity. This issue is particularly relevant for smaller lesions, in which the relative influence of reconstruction was greatest in our study. Consistent reconstruction settings may therefore be important when comparing quantitative measurements between examinations, particularly when evaluating changes in somatostatin receptor expression or treatment response. Krokos et al. evaluated the comparability of Q.Clear and OSEM reconstructions in 14 patients undergoing Ga-68 PET imaging and reported that β values of 800–1000 provided comparable semi-quantitative measurements between the two methods [22]. Although β600 provided favorable lesion uptake and contrast measurements, β800 and β1000 offered advantages in background noise suppression. The choice of penalization factor should consequently reflect the intended imaging objective rather than a single quantitative parameter. However, because visual lesion detectability and absolute quantitative accuracy were not independently evaluated, the clinical superiority of any individual reconstruction setting cannot be established from the present findings.

The present study has several strengths, including its prospective design, evaluation of 102 lesions across different size categories, and comparison of four reconstruction methods using identical acquisition datasets. Furthermore, the statistical approach accounted for repeated measurements and within-patient clustering, allowing a more appropriate assessment of reconstruction-dependent effects and their interaction with lesion size. Nevertheless, several limitations should be acknowledged. First, this single-center study included 45 patients examined using one PET/CT system, GE Discovery IQ 5-Ring, which may limit generalizability to other scanners and acquisition protocols. Second, the inclusion of different tumor types and lesion locations introduced potential heterogeneity in tracer uptake and background activity. Although SUVmax-based CNR was consistent with our quantitative objectives, its use may limit direct comparisons with studies employing SUVmean-based CNR definitions. Finally, the lack of a phantom-based reference standard precluded direct assessment of absolute quantitative accuracy. Additionally, the lack of a visual lesion detectability assessment limited our ability to determine whether improvements in quantitative parameters translated into better lesion detection. Further prospective, multicenter studies incorporating phantom measurements, visual image assessment, and different scanner technologies are needed to identify reconstruction settings that provide an appropriate balance between quantitative performance and image quality.

Conclusion

Q.Clear reconstruction significantly influences semi-quantitative parameters in Ga-68 DOTATATE PET/CT, with the magnitude of these effects depending on the selected penalization factor and lesion size. β600 provided higher lesion uptake and contrast measurements compared with conventional OSEM, whereas higher β values offered greater background noise suppression. Reconstruction-dependent SUVmax changes were particularly pronounced in smaller lesions, highlighting the importance of consistent reconstruction protocols for quantitative assessment. These findings support the need to balance lesion contrast and background noise when selecting Q.Clear reconstruction parameters for Ga-68 DOTATATE PET/CT.

Abbreviations

BMI: Body mass index
BPL: Bayesian penalized likelihood
CNR: Contrast-to-noise ratio
CT: Computed tomography
FDG: Fluorodeoxyglucose
IQR: Interquartile range
NET: Neuroendocrine tumor
OSEM: Ordered subsets expectation maximization
PET: Positron emission tomography
SBR: Signal-to-background ratio
SD: Standard deviation
SNR: Signal-to-noise ratio
SUV: Standardized uptake value
SUVmax: Maximum standardized uptake value
SUVmean: Mean standardized uptake value
TLR: Tumor-to-liver ratio
VOI: Volume of interest

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Institutional Review Board of Kartal Dr. Lütfı Kırdar City Hospital (Approval No. 2025/010.99/18/1). Written informed consent was obtained from all individual participants included in the study. All patient data were anonymized to ensure confidentiality.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated 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.

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Authors' contributions

SK contributed to data acquisition, data analysis, and manuscript preparation. FO contributed to the conception and design of the study. Both authors reviewed and approved the final manuscript and agree to be accountable for all aspects of the work.

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References

1. Sanli Y, Garg I, Kandathil A, Kendi T, Zanetti MJB, Kuyumcu S, et al. Neuroendocrine Tumor Diagnosis and Management: 68Ga-DOTATATE PET/CT. AJR Am J Roentgenol. 2018;211:267–77. 10.2214/AJR.18.19881.
2. Ting M, McDermott G, Zarei A, Patel C, Chowdhury FU, Rodrigues A, et al. Qualitative and quantitative analysis of reduced bed position acquisition time on FDG PET image quality. Nucl Med Commun. 2025;46:362–6. 10.1097/MNM.0000000000001957.
3. Ahn S, Ross SG, Asma E, Miao J, Jin X, Cheng L, et al. Quantitative comparison of OSEM and penalized likelihood image reconstruction using relative difference penalties for clinical PET. Phys Med Biol. 2015;60:5733–51. 10.1088/0031-9155/60/15/5733.
4. Springer S, Basset-Sagarminaga J, van de Weijer T, Schrauwen-Hinderling VB, Backes WH, Wierts R. Improving image reconstruction to quantify dynamic whole-body PET/CT: Q.Clear versus OSEM. EJNMMI Phys. 2025;12:27. 10.1186/s40658-025-00736-5.
5. Teoh EJ, McGowan DR, Macpherson RE, Bradley KM, Gleeson FV. Phantom and Clinical Evaluation of the Bayesian Penalized Likelihood Reconstruction Algorithm Q.Clear on an LYSO PET/CT System. J Nucl Med. 2015;56:1447–52. 10.2967/jnumed.115.159301.

6. Wang Y, Lin L, Quan W, Li J, Li W. Effect of Bayesian penalty likelihood algorithm on 18F-FDG PET/CT image of lymphoma. Nucl Med Commun. 2022;43:284–91. 10.1097/MNM.0000000000001516.
7. Wyrzykowski M, Siminiak N, Kaźmierczak M, Ruchała M, Czepczyński R. Impact of the Q.Clear reconstruction algorithm on the interpretation of PET/CT images in patients with lymphoma. EJNMMI Res. 2020;10:99. 10.1186/s13550-020-00690-6.
8. Murat H, Zulkifli MAA, Said MA, Awang Kechik M, Tahir D, Abdul Karim MK. Optimizing time-of-flight of PET/CT image quality via penalty β value in Bayesian penalized likelihood reconstruction algorithm. Radiography (Lond). 2025;31:343–9. 10.1016/j.radi.2024.12.011.
9. Özülker F, Babacan GB, Cengiz S, Özülker T. The effect of reconstruction algorithms on semi-quantitative measurements in 18F-FDG PET/CT imaging. Hell J Nucl Med. 2024;27:85–92. 10.1967/s002449912721.
10. Chicheportiche A, Goshen E, Godefroy J, Grozinsky-Glasberg S, Oleinikov K, Meirovitz A, et al. Can a penalized-likelihood estimation algorithm be used to reduce the injected dose or the acquisition time in 68Ga-DOTATATE PET/CT studies? EJNMMI Phys. 2021;8:13. 10.1186/s40658-021-00359-6.
11. Cox CPW, Segbers M, Graven LH, Brabander T, van Assema DME. Standardized image quality for 68Ga-DOTA-TATE PET/CT. EJNMMI Res. 2020;10:27. 10.1186/s13550-020-0601-y.
12. Long Q, Tian Y, Hu Y, Xu Z, Zhang W, Xu S, et al. Scanner-integrated reconstruction versus post-processing deep learning for low-count 18F-FDG PET/CT: a comparative clinical evaluation. EJNMMI Phys. 2026;13:20. 10.1186/s40658-026-00841-z.
13. Temple JA, Prem R. Optimising Gallium-68 (^{68}Ga) DOTATATE PET/CT Reconstruction in Neuroendocrine Tumours: A Paired Comparison of Penalised-Likelihood (BSREM/Q.Clear) and Ordered Subset Expectation Maximisation Algorithms. Cureus. 2025;17:95049. 10.7759/cureus.95049.
14. Caribé PRRV, Koole M, D'Asseler Y, Van Den Broeck B, Vandenberghe S. Noise reduction using a Bayesian penalized-likelihood reconstruction algorithm on a time-of-flight PET-CT scanner. EJNMMI Phys. 2019;6:22. 10.1186/s40658-019-0264-9.
15. Lindström E, Lindsjö L, Sundin A, Sörensen J, Lubberink M. Evaluation of block-sequential regularized expectation maximization reconstruction of 68Ga-DOTATOC, 18F-fluoride, and 11C-acetate whole-body examinations acquired on a digital time-of-flight PET/CT scanner. EJNMMI Phys. 2020;7:40. 10.1186/s40658-020-00310-1.
16. Zanoni L, Argalia G, Fortunati E, Malizia C, Allegri V, Calabrò D, et al. Can Q.Clear reconstruction be used to improve [68 Ga]Ga-DOTANOC PET/CT image quality in overweight NEN patients? Eur J Nucl Med Mol Imaging. 2022;49:1607–12. 10.1007/s00259-021-05592-w.
17. Di Franco M, Fortunati E, Zanoni L, Bonazzi N, Mosconi C, Malizia C, et al. β1600 Q.Clear Digital Reconstruction of [68Ga]Ga-DOTANOC PET/CT Improves Image Quality in NET Patients. J Clin Med. 2024;13:3841. 10.3390/jcm13133841.
18. Kurita Y, Ichikawa Y, Nakanishi T, Tomita Y, Hasegawa D, Murashima S, et al. The value of Bayesian penalized likelihood reconstruction for improving lesion conspicuity of malignant lung tumors on

18F-FDG PET/CT: comparison with ordered subset expectation maximization reconstruction incorporating time-of-flight model and point spread function correction. Ann Nucl Med. 2020;34:272–9. 10.1007/s12149-020-01446-x.

19. You H, Sanli Y, Subramaniam RM. Impact of Point-Spread Function Reconstruction on 68Ga-DOTATATE PET/CT Quantitative Imaging Parameters. AJR Am J Roentgenol. 2019;213:683–8. 10.2214/AJR.18.21067.
20. Liu L, Liu H, Xu S, Zhang S, Tao Y, Mok GSP, Chen Y. The Impact of Total Variation Regularized Expectation Maximization Reconstruction on 68Ga-DOTA-TATE PET/CT Images in Patients With Neuroendocrine Tumor. Front Med (Lausanne). 2022;9:845806. 10.3389/fmed.2022.845806.
21. Gavriilidis P, Koole M, Marinus A, Jansen FP, Deller TW, Mottaghy FM, et al. Performance evaluation of iterative PET reconstruction with resolution recovery incorporating Gallium-68 positron range correction. Med Phys. 2024;51:5927–42. 10.1002/mp.17259.
22. Krokos G, Pike LC, Cook GJR, Marsden PK. Standardisation of conventional and advanced iterative reconstruction methods for Gallium-68 multi-centre PET-CT trials. EJNMMI Phys. 2021;8:52. 10.1186/s40658-021-00400-8.

Figures

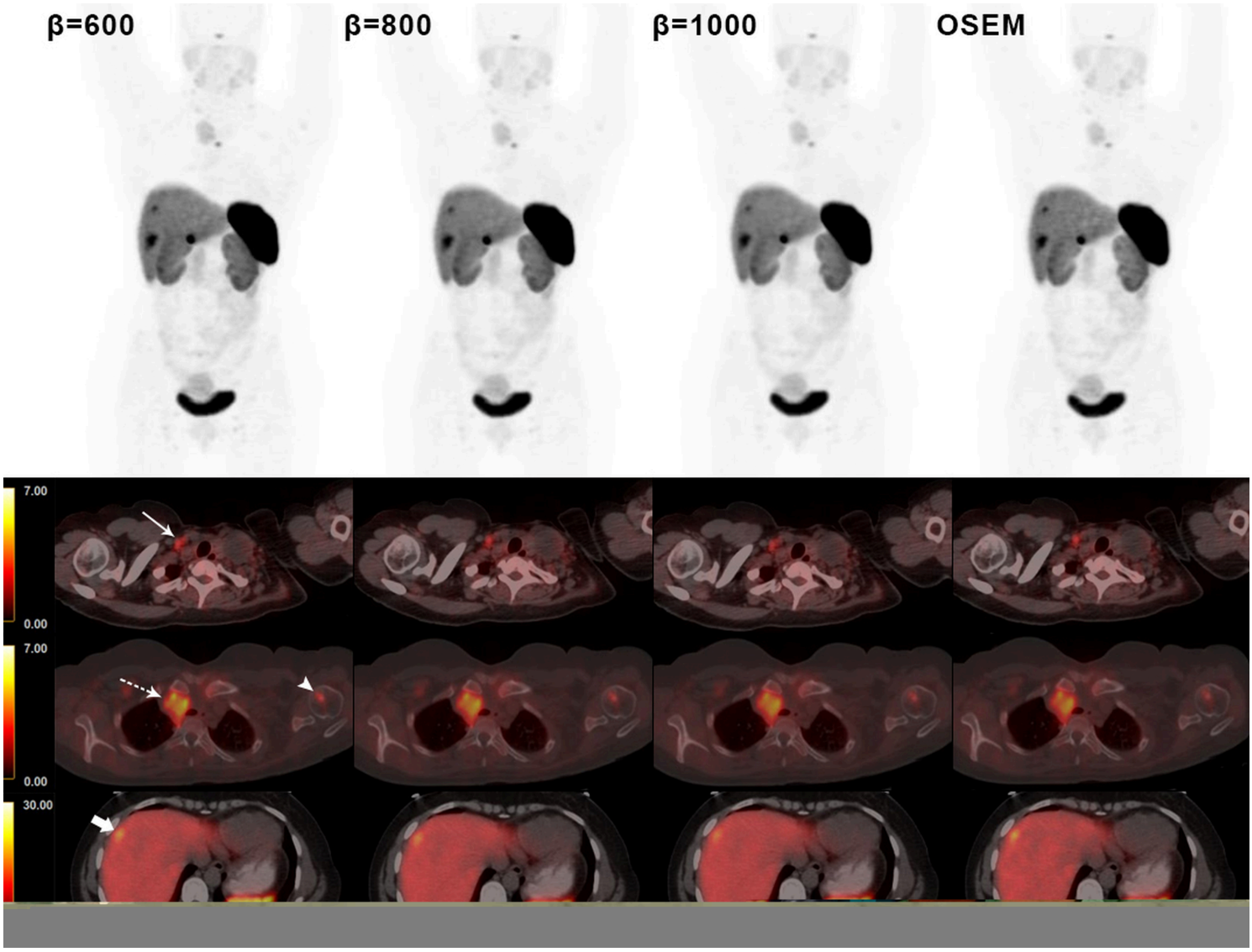


Figure 1

Representative Ga-68 DOTATATE PET/CT images of a patient with medullary thyroid carcinoma reconstructed using Q.Clear (β600, β800, and β1000) and conventional OSEM, displayed from left to right.