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Original Research Article

Evaluation of image resolution and quantification parameters on fdg-pet/ct images in patients with metastatic breast cancer using Q. clear and osem reconstruction techniques

Bimal Nepal[1], Tshetiz Dahal[2,*]

[1]*Dept. of Radiology, New STNM Multi-Speciality Hospital, Gangtok, Sikkim, India*
[2]*Dept. of Surgery and Medicine, Lugansk State Medical University, Ukraine*

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ABSTRACT

We compared the 2-[18F]FDG-PET/CT scans performed for response monitoring in patients with metastatic breast cancer in a prospective setting using the ordered subset expectation maximization (OSEM) algorithm and the bayesian penalized likelihood reconstruction algorithm (Q.Clear) and the image quality and quantification parameters. 35 patients with metastatic breast cancer who were treated and followed up with 2-[18F]FDG-PET/CT were included. A total of 150 scans were evaluated on a five-point scale for the image quality parameters of noise, sharpness, contrast, diagnostic confidence, artefact, and blotchy look while being blinded to the Q.Clear and OSEM reconstruction algorithms. In scans with detectable disease, the lesion with the highest volume of interest was chosen, taking into account both reconstruction techniques' interest levels. For the same heated lesion, SULpeak (g/mL) and SUVmax (g/mL) were contrasted. The OSEM reconstruction had significantly less blotchy appearance than the Q.Clear reconstruction, while there was no significant difference between the two methods in terms of noise, diagnostic confidence, or artefact. Q.Clear had significantly better sharpness ($p < 0.002$) and contrast ($p < 0.002$) than the OSEM reconstruction. Quantitative examination of 75/150 scans revealed that Q.Clear reconstruction considerably outperformed OSEM reconstruction in terms of SULpeak (6.33 ± 1.8 vs. 5.85 ± 1.5, $p < 0.002$) and SUVmax (7.27 ± 5.8 vs. 3.90 ± 2.8, p 0.002). In conclusion, OSEM reconstruction was less blotchy, but Q.Clear reconstruction showed superior sharpness, better contrast, higher SUVmax, and higher SULpeak.

1. Introduction

PET/CT, which combines positron emission tomography and integrated computed tomography, is frequently employed in the initial diagnosis, staging, and assessment of the therapeutic response to a variety of malignant disorders.[1] The development of hardware specifications and reconstruction techniques has increased imaging quality in PET/CT scanners, which has led to continual technical advancements.[2–4] The earlier generation of PET/CT systems based on analogue photo-multiplier tubes have been replaced by novel PET/CT scanners based on digital silicon photo-multiplier (SiPM) technology. In comparison to analogue PET/CT scanners,[3–6] this results in a significant improvement in image contrast and noise level,[7,8] which could lead to greater diagnostic accuracy and overall image quality. Under the brand name Q.Clear, a new reconstruction method utilising the block sequential regularized expectation maximization (BSREM) technique has been developed. When compared

* *Corresponding author*.
E-mail address: dahaltshetiz21@gmail.com (T. Dahal).

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to ordered subset expectation maximization (OSEM), this technique permits fully convergent iterative reconstruction, producing higher image contrast while suppressing noise.[9] As utilising the Q.Clear algorithm may raise the maximal standardised uptake (SUVmax) values within metastatic lesions compared to OSEM reconstruction,[10] advanced reconstruction approaches aim to improve not only the quality of imaging but also quantitative metrics.[5] 2-deoxy-2-[18F] fluoro-D-glucose Based on its outstanding sensitivity (above 95%) for detecting distant metastases, PET/CT (2-[18F]FDG-PET/CT) has been used more and more in metastatic breast cancer.[11] Utilising 2-[18F]FDG-PET/CT for response assessment may enhance clinical management and survival[12–14]. Quantitative PET/CT is crucial for evaluating tumour response objectively,[5] and the PET Response Criteria in Solid Tumours (PERCIST) have been proposed as practical and useful criteria for breast cancer.[15–17] According to earlier research, Q. Clear reconstruction is superior than OSEM reconstruction in terms of overall picture quality, contrast recovery, noise suppression, lesion detectability, and accurate quantification.[18–20] Before using the Q.Clear algorithm as a reconstruction method for semi-quantitative PERCIST investigations in clinical practise, more research contrasting the two reconstruction techniques in a clinical setting is necessary.[21] Thus, in a clinical context with patients undergoing response evaluation, we sought to compare the two reconstruction algorithms (Q.Clear vs. OSEM) in terms of the overall image quality and quantifying indicators during treatment for metastatic breast cancer.

2. Materials and Methods

2.1. Patients

Following the STROBE recommendation, a prospective comparison study was carried out in the Department of Radiology in the Apollo Hospital, Bangalore.[22] Patients in this study are a subset of a broader patient cohort that was examined in a larger prospective trial on response monitoring in metastatic breast cancer. Women with advanced breast cancer who were referred to the Department of Oncology (Apollo Hospital) between September 2020 and September 2021 and originally assessed with 2-[18F]FDG-PET/CT were deemed eligible. All participants completed written informed consent forms after the study protocol was approved by the Hospital Ethics Committee. The Declaration of Helsinki was followed in conducting the study, and Indian Radiology Medicine (IRM) guidelines were used to do all scans.[23] The following criteria were used to determine eligibility for this study: biopsy-verified relapsed or de novo metastatic breast cancer (biopsy verification of main tumour and disseminated disease at baseline scan), digital PET/CT imaging, and accessible clinico-histopathological data. Patients receiving treatment for other invasive malignancies and those under the age of 18 were excluded criteria.[24] Prior to the start of the treatment, baseline scans were conducted. Patients were monitored on the same PET/CT scanner and scanned in accordance with the standardization criteria recommended by PERCIST.[17] In accordance with Indian clinical recommendations, patients were imaged every 9 to 12 weeks. In the current analysis, the baseline, first follow-up, and second follow-up scans were all used. The same team of skilled doctors analyzed scans using the Q.Clear and OSEM reconstruction algorithms to compare overall image quality metrics, maximum standardised uptake value (SUVmax), and peak lean body mass corrected SUV (SULpeak).

3. PET/CT Imaging Protocol

On GE Discovery MI 4-ring PET/CT scanners with a 25 cm field of view, PET/CT data were collected. Using a normal whole-body (head-to-thigh) acquisition technique with slice overlaps of 50% and acquisition times of 1.5 min each bed position, PET scans were conducted 60 min following injection of 4 mBq/kg FDG (min 200 MBq, max 400 MBq). PET datasets were rebuilt using a time-of-flight 3D OSEM (GE VPFX, 4 iterations, 20 subsets) reconstruction method with point-spread function correction (GE SharpIR) and Q.Clear ($\beta = 250$) in 255×255 matrix sizes (pixel size 2.74 mm). Within the iterative loop, attenuation, dispersion, randoms, dead-time, and normalization corrections were made.The attenuation correction was performed utilising a specialised helical CT attenuation correction scan that was taken following the PET scan using a conventional CT protocol and a scan field of view of 70 cm. Trans-axial slices were created from the data using a conventional filter, with a field of view of 50 cm, a matrix size of 515×515 (pixel size 0.95 mm), and a slice thickness of 3.73 mm.[23]

4. Qualitative Image Analysis

Before examining the image quality, a senior nuclear medicine professional (M.H.V.) convened a clarifying session to guarantee that the interpreters were using the same methodology. Three skilled nuclear medicine specialists examined the Q.Clear and OSEM reconstruction algorithms' image quality parameters. Each scan was subjected to a physician's evaluation of the qualitative image analyses. While being blinded to the reconstruction methods, the same doctor simultaneously analysed two reconstruction approaches for six image quality parameters on two distinct screens (side by side). The following quality metrics were evaluated amongst the reconstruction techniques using a five-point scale (1 being the worst and 5 being the best; Table 1): noise, sharpness, contrast, diagnostic confidence, artefact, and blotchy look.[25] The doctors were skilled at separating the factors with overlap, such as noise, contrast, and sharpness, as well as evaluating

Table 1: Grading scale for subjective image quality evaluation

Parameters	5	4	3	2	1
Noise	Minimal or no noise	No significant noise	Noisy diagnostic	Significant noise (affects diagnosis)	High-level noise (non-diagnostic)
Sharpness	Excellent sharpness	Good sharpness	Moderate sharpness	Poor sharpness (bad visibility)	Zero visibility(non-diagnostic)
Contrast	Excellent contrast	Very good contrast	Good contrast	Poor contrast (unsatisfactory visualization)	Image similar to use of no contrast (non-diagnostic)
Diagnostic confidence	Completely confidence	High confidence	Good confidence	Poor confidence	No diagnostic confidence (unacceptable)
Artefact	No artefact	Insignificant artefact	Minor artefact	Major artefact (diagnosis still possible)	Artefact affecting diagnostic information
Blotchy appearance	Absent	Mild	Moderate	Significant (diagnosis still possible)	Intense (affecting diagnosis)

scan noise and grading the parameters on a subjective scale. The interpreters independently assessed the images and were familiar with the clinical significance of PET/CT.

5. Quantitative Image Analysis

Quantitative evaluations of PET/CT scans were performed. Using the same image number, the same volume of interest (VOI), and the PETVCAR automatic software (AW version 3.2, GE Healthcare, Chicago, IL, USA) in both reconstruction methods, the hottest lesion according to one-lesion PERCIST was chosen in scans with measurable disease. The maximum possible mean value of a 1 cm3 sphere in the VOI located within the metastatic lesions was referred to as SULpeak. Patients had their serum glucose levels evaluated to make sure they were under the PERCIST standards for acceptable levels (less than 200 mg/dL).[17] The maximal uptake in the VOI that represents the highest tissue concentration of FDG uptake in the tumour was designated as SUVmax. For SUVmax normalization, body weight and height were taken into account.[26] For the same warmest lesion, SULpeak (g/mL) and SUVmax (g/mL) were determined and compared. SULpeak and SUVmax were not evaluated for scans with a complete metabolic response, but quantification of FDG uptake was done on scans with quantifiable illness at baseline and for comparable scans during follow-up.

6. Outcome Measure and Statistical Analysis

Using the median (range) and mean standard deviation, continuous data were displayed. For categorical variables, frequencies and corresponding percentages were provided. The six criteria for the two algorithms' picture quality and the quantitative parameters (SULpeak and SUVmax) of the hottest lesion were compared using a t-test. The threshold for statistical significance was established at 0.05. The software STATA/IC (version 16.1, StataCorp, College Station, USA) was used for all statistical analyses.

7. Results

The analysis included 37 patients with a total of 63 follow-up scans, including first and second follow-up scans, and 37 baseline images. Figure 1 depicts a flowchart for the study. Table 2 provides a summary of the clinical and histological data for the patients that were included.

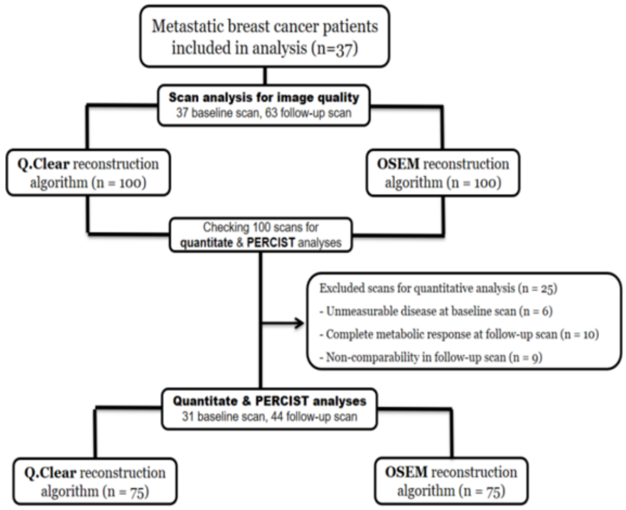

Fig. 1: Study flowchart for image quality and quantitative analyses (OSEM: ordered subset expectation maximization; Q. Clear: Refers to the reconstruction algorithm using block sequential regularized expectation maximization; PERCIST: PET Response Criteria in Solid Tumors).

Comparing the parameters related to the quality of images, Q.Clear had significantly better sharpness (mean scores of 4.65 vs. 3.91) and contrast (mean scores of 4.23 vs.

Table 2: Clinicopathological characteristics of included patients with metastatic breast cancer.

Characteristics		**Results ***
Age (years)		71.9 (45.9–91.1)
Primary cancer treatment	Postoperative adjuvant treatment	24 (64.7)
	Adjuvant and neoadjuvant treatments	3 (8.1)
	No treatment/unknown	10 (27.0)
	History of radiotherapy	24 (64.7)
Primary disseminated cancer		12 (32.4)
Histopathology	Adenocarcinoma	28 (75.7)
	Invasive ductal carcinoma	5 (13.5)
	Invasive lobular carcinoma	4 (10.8)
Positive estrogen receptor		32 (86.5)
Negative Herceptin receptor		34 (91.9)
Origin of biopsy **	Bone	13 (35.1)
	Liver	7 (18.9)
	Lung	1 (2.7)
	Lymph nodes	6 (16.2)
	Breast	10 (27.0)
First-line treatment	Endocrine therapy	5 (13.5)
	Endocrine therapy + CDK4/6 inhibitor	24 (64.9)
	Chemotherapy	4 (10.8)
	Others	4 (10.8)

4.10) compared with the OSEM reconstruction ($p < 0.001$ and $p = 0.001$, respectively), while there was no significant difference regarding noise, diagnostic confidence, and artefact when comparing the two reconstruction methods. The OSEM reconstruction had less blotchy appearance (4.57 vs. 4.34) compared with Q.Clear reconstruction ($p < 0.001$). Scores related to imaging quality parameters are summarized in Table 3. An example of 2-[18F]FDG-PET/CT, comparing the sharpness and contrast using OSEM and Q.Clear reconstructions, respectively, is shown in Figure 2.

A total of 31/37 (84%) patients had measurable disease at baseline (Figure 1), for whom quantitative analysis was performed on the hottest lesion according to the PERCIST criteria. At follow-up scans, quantitative analyses were performed in 44/63 (70%) scans being comparable according to the PERCIST criteria. Q. Clear reconstruction had significantly higher SULpeak (5.33 ± 2.8 vs. 4.85 ± 2.5, $p < 0.001$) and SUVmax (8.27 ± 4.8 vs. 6.90 ± 3.8, $p < 0.001$) compared with the OSEM reconstruction (Table 4). When comparing the two reconstruction methods for change

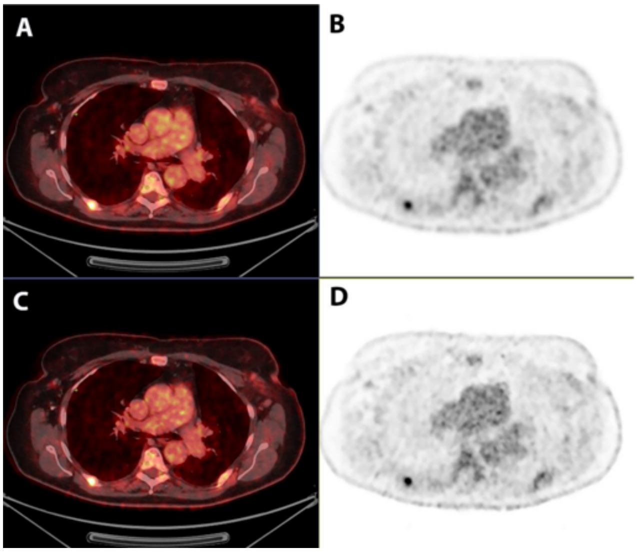

Fig. 2: 2-[18F]FDG-PET/CT scan for a patient with metastatic breast cancer, illustrating the sharpness and contrast via OSEM and Q.Clear reconstructions ((A,B) OSEM reconstruction vs. (C,D) Q.Clear reconstruction).

Table 3: Scores of image quality parameters within the OSEM and Q.Clear reconstruction methods.

Characteristics	**OSEM ***	**Q.Clear ***	**Mean Difference (95% CI)**	**p - Value**
Noise	4.41 ± 0.55	4.42 ± 0.54	0.01 (−0.16–0.14)	0.88
Sharpness	3.91 ± 0.49	4.65 ± 0.59	−0.74 (−0.83–−0.65)	<0.001
Contrast	4.1 ± 0.66	4.23 ± 0.74	−0.13 (−0.22–−0.04)	0.001
Diagnostic confidence	4.52 ± 0.70	4.52 ± 0.69	0 (−0.28–0.28)	0.99
Artifacts	4.37 ± 0.68	4.38 ± 0.66	−0.01 (−0.3–0.01)	0.32
Blotchy appearance	4.57 ± 0.57	4.34 ± 0.59	0.23 (0.12–0.34)	<0.001

OSEM: ordered subset expectation maximization; CI: confidence interval; Q.Clear: refers to the reconstruction algorithm using block sequential regularized expectation maximization (BSREM). * Image quality scores (mean ± standard deviation) are reported using a five-scale questionnaire (1 = worst and 5 = best).

in SULpeak and SUVmax between the two following scans, there was no significant difference in the median SULpeak changes, while the median SUVmax changes were significantly higher for Q.Clear reconstruction.

8. Discussion

On the basis of quantitative analysis of 2-[18F]FDG-PET/CT scans of patients with metastatic breast cancer and image quality metrics, a prospective comparison of the OSEM and Q.Clear reconstruction algorithms

Table 4: Quantitative analysis within the hottest lesion via OSEM and Q.Clear reconstruction methods.

Characteristics	OSEM *	Q.Clear *	Mean Difference (95% CI)	p-Value
SUL peak				
Baseline scans	5.82 (1.4–12.12)	6.84 (1.61–12.95)	−0.6 (−0.82–−0.39)	<0.001
Follow-up scans	3.01 (1.65–11.01)	3.47 (1.79–12.82)	−0.39 (−0.52–−0.26)	0.001
All scans	4.3 (1.4–12.12)	4.63 (1.61–12.95)	−0.47 (−0.59–−0.36)	<0.001
Change to 1st follow-up	1.94 (0.07–5.71)	1.95 (0–5.86)	0.04 (−0.24–0.33)	0.75
Change to 2nd follow-up	0.53 (0.02–4)	0.8 (0.05–4.16)	0.12 (−0.23–0.26)	0.1
SUVmax				
Baseline scans	8.12 (2.0–18.42)	9.46 (2.37–24.86)	−1.49 (−1.97–1.01)	<0.001
Follow-up scans	4.61 (2.22–18.42)	5.48 (2.47–24.86)	−1.25 (−1.73–−0.77)	0.005
All scans	6.16 (2.0–18.42)	7.15 (2.37–24.86)	−1.35 (−1.69–−1.01)	<0.001
Change to 1st follow-up	2.34 (0–8.3)	2.39 (0–9.5)	0.45 (0.10–0.79)	0.01
Change to 2nd follow-up	1.1 (0.05–4.92)	1.5 (0.26–11.2)	0.89 (0.20–1.58)	0.04

OSEM: ordered subset expectation maximization; CI: confidence interval; Q.Clear: refers to the reconstruction algorithm using block sequential regularized expectation maximization (BSREM); SUVmax: maximum standardized uptake value; SULpeak: peak lean body mass corrected SUV. * Data are shown as the median (range).

was made. The OSEM reconstruction had less of a "blotchy appearance" than the Q.Clear reconstruction, which may be due to OSEM reconstruction's lower noise level. The Q.Clear reconstruction greatly outperformed an OSEM reconstruction in terms of sharpness and contrast. With Q.Clear reconstruction, registered SULpeak and SUVmax values were much greater than with OSEM reconstruction. SULpeak values changed over the follow-up period regardless of the reconstruction technique, whereas SUVmax values changed much more with the Q.Clear reconstruction. Our study found that Q.Clear reconstruction produced images with better contrast and sharpness than OSEM reconstruction, which is consistent with the findings of other studies showing the superiority of BSREM-based reconstruction methods over OSEM reconstruction.[27,28] Using a 4 mm Gaussian filter frequently in OSEM reconstruction smoothed the blotchy look and produced higher picture quality, while a missing Gaussian filter may cause a more "blotchy appearance" on Q.Clear images.[28] We discovered no difference in the diagnostic certainty between the two reconstruction techniques, suggesting that any of them may be selected for clinical use. Similar investigations have also found that Q.Clear produces images with improved overall quality when compared to OSEM in PET/CT scans using [68Ga]Ga-DOTANOC,[29] 18F-fluciclovine.[20] and [68Ga]Ga-PSMA.[30] This demonstrates that Q.Clear's enhanced image quality is not restricted to 2-[18F]FDG-PET/CT scans. Furthermore, according to a few studies, Q.Clear produced images with higher picture quality than OSEM during PET/MR scans.[2,18,31] The cause might be the same as in PET/CT scans, assuming OSEM reconstruction was unable to fully reach convergence because of greater noise and longer iteration periods. To guarantee the preferred β value of reconstructions ensuring the best picture quality, more investigations using phantom data are required.[20.29,30]

The Q.Clear algorithm's improved image quality may be due to the fact that it decreases noise by acting like an adaptive filter with adjustable filter width and enhances contrast by enhancing quantification, both of which together have the impact of boosting image quality. This is consistent with our findings, which show that Q.Clear reconstructions have better contrast, enabling full convergence without the excessive typical OSEM noise.[29] This essentially reduces the OSEM algorithm's iterations in order to prevent the image from having too much noise, which would prevent convergence and reduce visual contrast.[2] On the other hand, thanks to the noise regularization, Q.Clear can reach full convergence, leading to improved resolution and more accurate quantitative measurements.[19,32] The results of earlier studies, which showed that Q.Clear allows a significant increase in quantitative parameters and better reflects the true uptake,[9,20] are consistent with the absolute values of SUVmax and SULpeak within the OSEM and Q.Clear reconstruction algorithms. Since quantification-based tests (like the PERCIST analysis) can be used in clinical practise as well as for research, Q.Clear has the potential to offer better quantification accuracy. The Q. Clear reconstruction offers a higher SUVmax for suspected lymph node metastases than the OSEM reconstruction, according to Lundeberg et al.'s comparison of the two reconstruction modalities on lung cancer patients in a clinical context. Higher SUVmax values did not, however, increase the ability to detect metastatic lesions.[33] Our findings also demonstrated that, unlike SUVmax, for which changes were higher for the Q.Clear than OSEM reconstruction, SULpeak changes over the follow-up period were not related to the reconstruction algorithm, demonstrating SULpeak's robustness for PERCIST analysis across reconstruction algorithms. This is consistent with the suggested upward bias for SUVmax using a single pixel, despite PERCIST's recommendation to use a larger region of interest by SULpeak[17] because the size of a single voxel may vary significantly among PET/CT scans, resulting in different noise levels in the metric and various filtering.

Additionally, Q.Clear demonstrated a clinically applicable recovery coefficient for sphere sizes ranging from 10 to 37 mm, which is advantageous for the detection of lesions and is more consistent with the quantification of lesions in accordance with PERCIST criteria.[34] Additionally, PERCIST has been shown to have a high degree of application,[16] a greater level of overall interrater agreement and reliability compared to a qualitative assessment,[35,36] and to be more effective at detecting new lesions or unmistakable advancement in non-target lesions.[37] As a result, practical use of the PERCIST assessment may enhance prognostic stratification[15,37,38] and offer a consistent methodology independent of interpreters and reconstruction techniques.According to the PERCIST criteria, a variation in the absolute value of SULpeak may lead to different response categories, which could ultimately have an impact on the treatment strategy for the patient. Therefore, through enhanced quantification accuracy, a clinical indication of the Q.Clear reconstruction algorithm may result in a more accurate therapy monitoring by PET/CT.[39] However, it has been observed that the Q.Clear algorithm's clinical indication in the treatment evaluation of lymphoma patients is ambiguous, which could be accounted for by its incompatibility with the recommended practices.[10] Therefore, for Q.Clear to have a major impact on patient management, compatibility with current recommendations must be established prior to the algorithm's introduction into clinical practise.

The inclusion of clinical follow-up of patients with metastatic disease, which represents standard clinical practise, was a strength of this study. Furthermore, strict adherence to standardization requirements like the PERCIST principles was observed when using the PERCIST criteria for response monitoring and quantification of FDG uptake.[17] In order to exclude the impacts of scanner variance, patients were monitored on the same type of scanner while comparing quantitative data between follow-up scans. The same doctor evaluated both reconstruction techniques side-by-side while being blinded to the reconstruction methods as the interpreters for image quality measures. Because only one operator evaluated each scan, our visual comparison of overall image quality was limited and could have been skewed by the translator physician's personal preferences. Additionally, measurements of the size and quantity of the discovered lesions for the two reconstruction techniques would have improved the outcomes of the quantitative analyses. The findings of the current investigation could be validated by subsequent multicenter studies on a greater number of scans examined by numerous skilled nuclear medicine doctors. The two reconstruction techniques' lesion-based accuracy and the possible impact on response categories are still open questions. Future research should also take into account the best penalization factor (-value) for clinical application and phantom measurements related to Q.Clear.

9. Conclusion

Q. Compared to OSEM reconstruction, clear reconstruction had much superior sharpness and contrast, whereas OSEM reconstruction's blotchy appearance was less noticeable. The two reconstruction algorithms have equivalent diagnostic confidence, making them equally suitable for routine clinical practise. In terms of quantitative measurements, the Q.Clear method outperformed OSEM reconstruction with greater SUVmax and SULpeak. Regardless of the reconstruction approach, SULpeak alterations at follow-up scans remained independent of it, showing that SULpeak is reliable for PERCIST analysis.

10. Institutional Review Board Statement

The study protocol was approved by the Apollo Hospital Ethics Committee in Bangalore, India.

11. Informed Consent Statement

Written informed consent was obtained from the patients to use their data and publish this paper.

12. Data Availability Statement

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

13. Source of Funding

None.

14. Conflicts of Interest

The other authors declare no conflict of interest.

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Author biography

Bimal Nepal, Imaging Technologist, Research Scholar

Tshetiz Dahal, General Physician and Clinical Researcher https://orcid.org/0000-0002-4042-7768

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