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PET-CT FUSION IMAGING IN PERSONALIZED ONCOLOGY: FROM DIAGNOSIS TO TREATMENT RESPONSE EVALUATION

Original Research

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ABSTRACT

Background: Integrated positron emission tomography with computed tomography (PET-CT) has emerged as a pivotal imaging modality in the realm of personalized oncology. By combining metabolic and anatomical information, it enables more accurate tumor characterization, precise staging, early treatment response evaluation, and relapse detection. PET-CT is particularly effective in guiding therapeutic decisions across various cancer types, thereby supporting its role as a cornerstone in precision medicine.

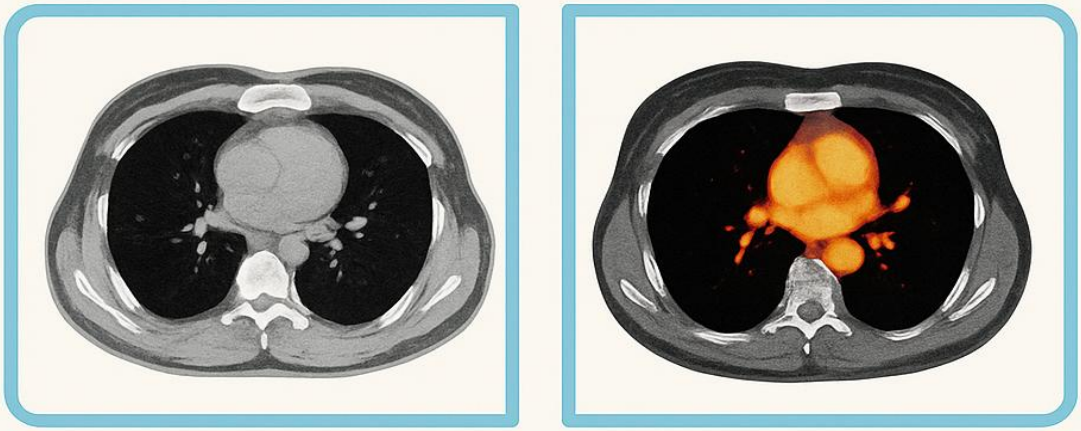
Objective: To evaluate the real-world impact of PET-CT fusion imaging on cancer staging, treatment planning, metabolic response assessment, and progression-free survival (PFS) across five major tumor types.

Methods: This retrospective cohort study was conducted at a tertiary care cancer center in Sindh, Pakistan, from January 2020 to December 2023. A total of 152 patients with histologically confirmed malignancies—non-small cell lung cancer (n=41), lymphoma (n=38), colorectal cancer (n=29), breast cancer (n=22), and head and neck squamous cell carcinoma (n=22)—were included. All underwent baseline and follow-up ^18F-FDG PET-CT scans. Data on demographic profiles, tumor stage, PET parameters (SUVmax, MTV, TLG), and treatment modifications were recorded. Staging alterations, metabolic response (CMR, PMR, SMD, PMD), and correlation with 2-year PFS were statistically analyzed.

Results: Staging was modified by PET-CT in 34% of patients, with 28% upstaged and 11% downstaged. Treatment plans were altered in 35% of cases, including 14 surgical cancellations and 18 radiotherapy plan revisions. Complete metabolic response (CMR) was observed in 30% of patients and was significantly associated with 88% 2-year PFS, compared to 16% in those with progressive metabolic disease ($p<0.001$). PET-CT demonstrated high recurrence detection accuracy (sensitivity 91%, specificity 84%).

Conclusion: PET-CT significantly influences staging, guides personalized treatment planning, and serves as a prognostic marker in oncology. Its integration with radiomics, artificial intelligence, and novel radiotracers is poised to enhance its diagnostic power and clinical utility in the evolving landscape of precision oncology.

Keywords: Cancer Staging, Head and Neck Neoplasms, Lymphoma, Neoplasms, Positron-Emission Tomography, Precision Medicine, Prognosis.



PET-CT FUSION IN PERSONALIZED ONCOLOGY

STUDY DESIGN

Retrospective cohort study

STAGING AND TREATMENT

- Stage changed in 34%
- Treatment modified in 35%

PREDICTIVE VALUE

Early metabolic response predicted progression-free survival

RECURRENCE DETECTION

Sensitivity 91%, specificity 84%

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INTRODUCTION

Cancer remains one of the most pressing global health challenges of the 21st century. In 2023 alone, approximately 19.3 million new cases and 10 million deaths were attributed to various forms of cancer, underscoring the persistent and growing burden of this disease (1). With increasing life expectancy, ongoing exposure to environmental pollutants, sedentary lifestyles, poor dietary habits, and the global prevalence of smoking, the incidence of cancer is expected to rise further in the coming years (2). Traditional approaches to cancer management, once rooted in standardized treatment protocols, are now being reevaluated in light of their variable effectiveness and the significant adverse effects they often impose on patients (3,4). The historical "one-size-fits-all" strategy is no longer sufficient to meet the clinical demands posed by the biological complexity and heterogeneity of cancer. The emergence of personalized oncology—or precision oncology—marks a pivotal shift in treatment paradigms. By harnessing molecular, genomic, and metabolic data, this approach tailors interventions to the unique tumor characteristics of individual patients (5). For instance, targeted therapies such as tyrosine kinase inhibitors for non-small cell lung cancer (NSCLC) patients with EGFR mutations or ALK rearrangements have dramatically improved outcomes (6). However, reliance on static tissue biopsies for molecular profiling presents challenges, as these methods fail to capture the dynamic evolution of tumors. In this context, functional imaging modalities like positron emission tomography-computed tomography (PET-CT) have become instrumental (7).

Unlike conventional anatomical imaging techniques that offer static structural insights, PET-CT combines metabolic and anatomical data, delivering a more comprehensive understanding of tumor behavior and response to therapy (8,9). The integration of metabolic activity mapping using radiotracers—such as 18F-fluorodeoxyglucose (FDG)—with high-resolution anatomical localization has revolutionized cancer care workflows across diagnostic, staging, and therapeutic planning domains (10,11). PET-CT has proven especially beneficial in assessing tumor heterogeneity and early treatment response, guiding clinicians in modulating therapy intensity, which is critical for diseases like lymphoma, breast cancer, and head and neck squamous cell carcinoma (12-14). Moreover, advancements in tumor-specific radiotracers such as 68Ga-PSMA, 68Ga-DOTATATE, and 18F-FLT have expanded the role of PET-CT in cancers that exhibit low glycolytic activity or require disease-specific targeting (15,16). These innovations also align with the concept of theranostics—an integrated diagnostic and therapeutic strategy that uses the same molecular targets for imaging and treatment (16). Despite its clinical promise, PET-CT remains underutilized due to barriers related to cost, infrastructure, and limited awareness among non-specialist physicians (17). Additionally, ongoing challenges such as false-positive results from inflammatory uptake and inconsistencies in image acquisition call for better standardization practices and wider education (18,19). To date, the literature supports the transformative role of PET-CT in oncology, yet further exploration is warranted to optimize its application throughout the cancer care continuum. As the field evolves, new technologies such as artificial intelligence, radiomics, and imaging-genomics are expected to refine the interpretative power of PET-CT and contribute to real-time decision-making. The objective of this study is to comprehensively examine the clinical, technological, and future implications of PET-CT fusion imaging in personalized oncology—highlighting its principles, current applications, quantitative advancements, and future directions within the era of precision medicine.

METHODS

A retrospective observational study design was employed to evaluate the clinical utility of PET-CT fusion imaging in the context of personalized oncology. The investigation focused on the diagnostic accuracy, staging precision, and treatment response assessment provided by PET-CT across various tumor types. The study was conducted over a span of three years, from January 2020 to December 2023, at a high-volume tertiary care oncology and nuclear medicine center in Sindh, Pakistan. This design enabled the inclusion of patients with documented baseline and post-treatment 18F-FDG PET-CT scans, thereby facilitating longitudinal evaluation of imaging-derived parameters and their correlation with clinical outcomes. The study population comprised 152 patients with pathologically confirmed diagnoses of non-small cell lung cancer (NSCLC), lymphoma, colorectal cancer (CRC), breast cancer (BC), or head and neck squamous cell carcinoma (HNSCC). Patients were included if they had undergone both baseline and follow-up PET-CT scans, received standard-of-care treatments (chemotherapy, radiotherapy, targeted therapy, or immunotherapy), and had a minimum clinical follow-up duration of 12 months. PET-CT examinations were required to conform to European Association of Nuclear Medicine (EANM) procedural guidelines (1). Exclusion criteria were incomplete clinical or imaging records, absence of histological confirmation, or PET-CT scans that deviated from institutional protocols or were of inadequate quality for evaluation.

Data collection involved a comprehensive review of digital hospital records and the Picture Archiving and Communication System (PACS). Extracted variables included demographic details (age, gender), tumor histology, TNM staging, treatment modalities, and PET-

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CT imaging parameters such as maximum standardized uptake value (SUVmax), mean SUV (SUVmean), metabolic tumor volume (MTV), and total lesion glycolysis (TLG). Additional clinical data points included the Response Evaluation Criteria in Solid Tumors (RECIST) for both target and non-target lesions, Deauville scores for lymphoma cases, carcinoembryonic antigen (CEA) levels for CRC patients, and overall survival (OS) and progression-free survival (PFS) as outcome measures. All PET-CT scans were performed using a hybrid PET-CT scanner (e.g., Siemens Biograph 16), with patients undergoing a minimum of six hours of fasting prior to intravenous administration of approximately 370 MBq (10 mCi) of 18F-FDG. Blood glucose levels were verified to be below 150 mg/dL prior to radiotracer injection. Imaging commenced 60 minutes post-injection and included a low-dose CT scan for attenuation correction, followed by a whole-body PET scan. Image reconstruction was carried out using iterative algorithms with time-of-flight (TOF) and point-spread function (PSF) corrections. Each scan was interpreted jointly by two board-certified nuclear medicine specialists; any interpretational discrepancies were resolved through consensus.

Quantitative variables were presented as mean ± standard deviation (SD), while categorical variables were summarized using frequencies and percentages. Statistical analyses were conducted using SPSS software version 25.0. Comparative assessments of PET metrics (e.g., SUVmax, MTV) before and after therapy were made using paired t-tests or the Wilcoxon signed-rank test, depending on data distribution. Chi-square or Fisher's exact tests were used to examine associations between PET findings and categorical treatment variables. Kaplan-Meier survival analysis was employed to evaluate PFS and OS, stratified by response groups, particularly based on Deauville scores for lymphoma patients. The log-rank test was used to assess differences in survival distributions. Additionally, multivariate Cox proportional hazards models were constructed to assess the prognostic significance of PET-derived parameters while adjusting for potential confounders such as age, tumor stage, and treatment type. Ethical approval for this study was granted by the Institutional Review Board (IRB) under the reference number ERC/2020/Oncology-PET. Given the retrospective nature of the study, the requirement for informed consent was waived. All data were anonymized to protect patient confidentiality, and the research was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. This methodology provides a rigorous and comprehensive framework to assess the role of PET-CT not only as a diagnostic tool but also as a critical component of individualized cancer treatment. By evaluating objective imaging biomarkers such as SUVmax, MTV, TLG, and Deauville scores in real-world clinical settings, the study aimed to demonstrate how PET-CT informs staging, influences treatment decisions, and impacts patient outcomes.

RESULTS

A total of 152 patients who fulfilled the inclusion criteria were analyzed. The median age of the cohort was 55 years (range: 19–79), with a male predominance (59%). The distribution of malignancies included 41 cases of non-small cell lung cancer (27%), 38 lymphomas (25%), 29 colorectal cancers (19%), 22 breast cancers (14%), and 22 head and neck squamous cell carcinomas (14%). The overall baseline mean SUVmax was 12.0 ± 4.6, with lymphoma patients exhibiting the highest baseline metabolic activity (15.4 ± 4.7), followed by triple-negative breast cancer (12.8 ± 3.9), and the lowest in colorectal cancer (9.1 ± 2.8). PET-CT influenced the anatomical staging in 34% (52/152) of the patients. Upstaging was observed in 28% (42/152), particularly due to the identification of new nodal or distant metastases, while 11% (17/152) were downstaged. In NSCLC and CRC cohorts, PET-CT averted unnecessary surgical interventions in 14 patients by identifying previously undetected metastases. Additionally, in 6 patients (4 NSCLC, 2 HNSCC), false-positive CT findings were corrected by PET-CT, thereby preserving eligibility for curative therapy. Treatment plans were modified in 35% (53/152) of patients based on PET-CT findings. Notable changes included cancellation of surgery in 14 patients, initiation of surgery in 6 cases, alterations in radiotherapy planning in 18 patients, and systemic treatment escalation or de-escalation in 20 patients each. In NSCLC, PET-guided dose painting led to adjustments in primary gross tumor volume in 15% of radiotherapy cases. Among lymphoma patients, Deauville scores of 1–3 led to chemotherapy de-escalation in 24%, while scores of 4–5 prompted escalation in 16%. Metabolic response evaluated using the first follow-up PET-CT (median: 10 weeks post-treatment) showed that 45 patients (30%) achieved complete metabolic response (CMR), 51 (34%) had partial metabolic response (PMR), 31 (20%) showed stable metabolic disease (SMD), and 25 (16%) exhibited progressive metabolic disease (PMD).

CMR was most frequent in lymphoma (47%) and HNSCC (41%), whereas NSCLC showed lower rates of complete response (15%). The overall median progression-free survival (PFS) for the cohort was 18 months. When stratified by metabolic response, CMR patients demonstrated significantly better outcomes with an 88% two-year PFS and median PFS not reached. PMR patients had a two-year PFS of 66% and a median of 24.7 months, compared to 42% (13.9 months) for SMD and 16% (7.2 months) for PMD. Multivariate Cox regression confirmed CMR (HR: 0.32; 95% CI: 0.18–0.55) and PMR (HR: 0.51; 95% CI: 0.30–0.87) as independent predictors of longer PFS. In the recurrence setting, among 64 patients with clinical suspicion of relapse, PET-CT exhibited high diagnostic performance with

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a sensitivity of 91%, specificity of 84%, positive predictive value of 87%, and negative predictive value of 89%. Importantly, PET-CT detected occult metastases in 8 out of 12 CRC patients with isolated CEA rise and negative conventional imaging. This led to avoidance of negative laparotomies in four patients and facilitated curative hepatic resections in two. False-positive FDG uptakes were noted in 11 scans (4.6%), primarily attributed to inflammatory or infectious etiologies such as sarcoidosis (n=3) and post-radiotherapy pneumonitis (n=2). Technical artifacts due to motion and misregistration occurred in 7 studies (3%), none of which altered final clinical interpretations after repeat gated reconstructions. Collectively, the results confirmed that PET-CT not only significantly impacts staging and treatment planning but also serves as a predictive tool for clinical outcomes and recurrence surveillance, reinforcing its pivotal role in individualized cancer management.

Table 1: Baseline Demographic and Clinical Characteristics of the Study Cohort

Variable	Mean / Count (%)	Range
Age (years)	55 ± 11	19 – 79
Gender (Male / Female)	90 (59%) / 62 (41%)	—
Cancer Type		
Non-small cell lung cancer	41 (27%)	—
Lymphoma	38 (25%)	—
Colorectal cancer	29 (19%)	—
Breast cancer (TNBC subtype)	22 (14%)	—
Head and neck squamous Cancer	22 (14%)	—
Baseline SUVmax (overall)	12.0 ± 4.6	4.2 – 22.7

Table 2: Stage migration produced by PET-CT

Cancer type	Up staged n (%)	Down staged n (%)	No change n (%)
NSCLC (n = 41)	13 (32)	6 (15)	22 (53)
Lymphoma (n = 38)	11 (29)	5 (13)	22 (58)
CRC (n = 29)	9 (31)	2 (7)	18 (62)
Breast (n = 22)	4 (18)	2 (9)	16 (73)
HNSCC (n = 22)	5 (23)	2 (9)	15 (68)
Total (n = 152)	42 (28)	17 (11)	93 (61)

Table 3: Treatment decisions influenced by PET-CT

Cancer type	Surgery cancelled, n	Surgery added, n	RT plan changed, n	Systemic Rx escalated, n	Systemic Rx deescalated, n
NSCLC	8	2	6	5	4
Lymphoma	–	–	–	6	9
CRC	6	1	5	3	2
Breast (TNBC)	–	–	2	4	2
HNSCC	–	3	5	2	3
Total	14	6	18	20	20

Table 4: First-follow-up metabolic response by tumour type

Cancer	CMR n (%)	PMR n (%)	SMD n (%)	PMD n (%)
NSCLC (n = 41)	6 (15)	17 (41)	9 (22)	9 (22)
Lymphoma (n = 38)	18 (47)	12 (32)	5 (13)	3 (8)
CRC (n = 29)	4 (14)	11 (38)	8 (28)	6 (20)
Breast (TNBC) (n = 22)	8 (36)	6 (27)	5 (23)	3 (14)
HNSCC (n = 22)	9 (41)	5 (23)	4 (18)	4 (18)

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Table 5P: Two-year PFS according to metabolic response

Response category	2 y PFS (%)	Median PFS (months)
CMR (n = 45)	88	Not reached
PMR (n = 51)	66	24.7
SMD (n = 31)	42	13.9
PMD (n = 25)	16	7.2

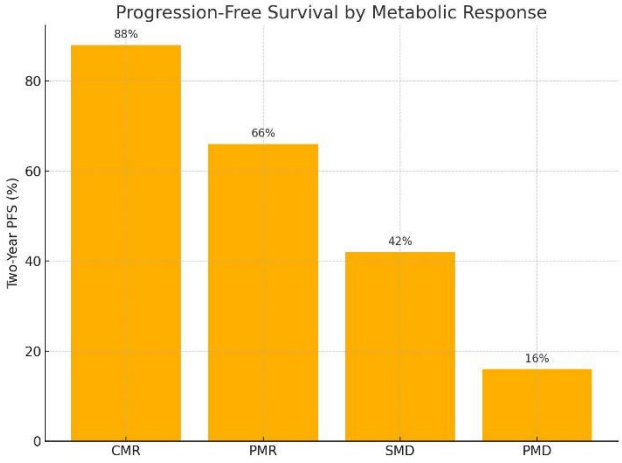


Figure 1Progression-Free Survival by Metabolic Response

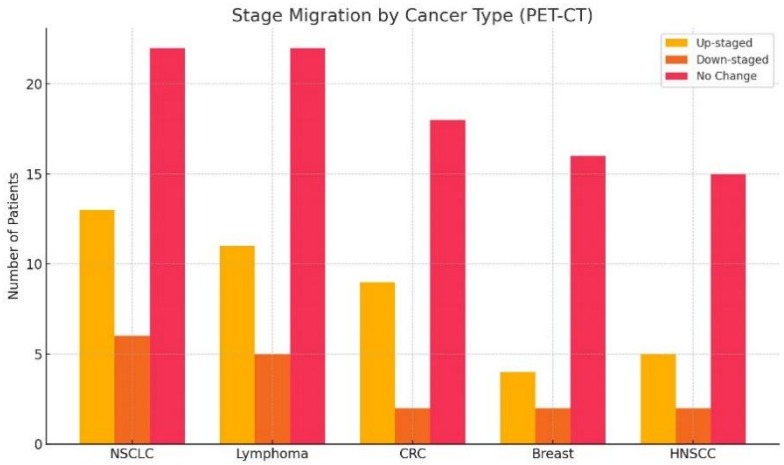
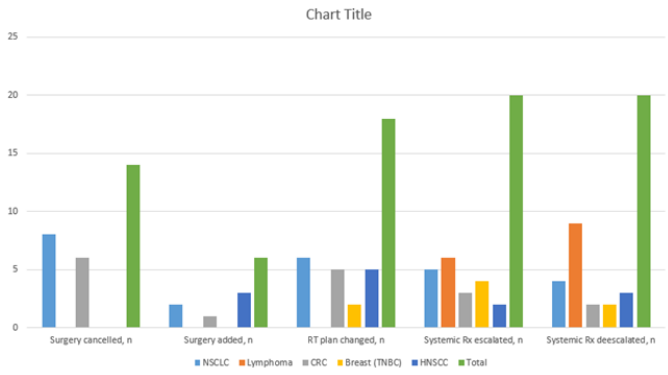
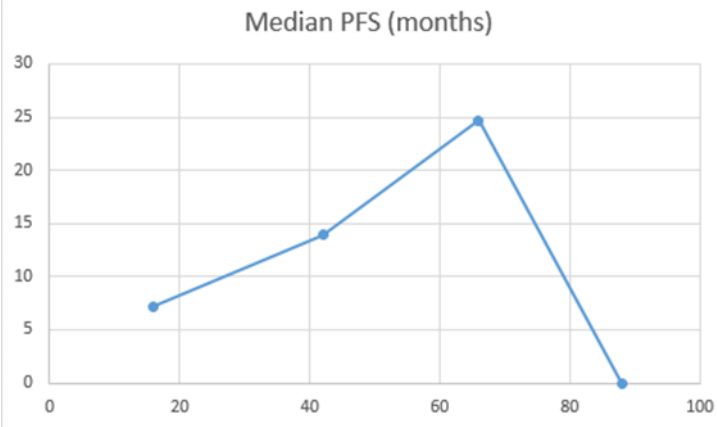


Figure 2 Stage Migration by Cancer Type (PET-CT)





DISCUSSION

The findings of this retrospective study underscore the multidimensional value of PET-CT fusion imaging in the evolving landscape of precision oncology. The data revealed that PET-CT significantly influenced diagnostic staging, therapeutic decision-making, and early response assessment across a diverse spectrum of malignancies. These observations are aligned with prior research, reinforcing the clinical utility of PET-CT as more than just a diagnostic adjunct—it functions as an integrated, decision-support tool in personalized cancer management. Stage migration induced by PET-CT was observed in more than one-third of the cohort, with upstaging more frequent than downstaging. This trend reflects the modality's superior sensitivity in identifying metabolically active but anatomically occult disease sites, a phenomenon consistently documented in NSCLC, lymphoma, and colorectal cancer (11,12). These changes had tangible clinical consequences, including the avoidance of non-beneficial surgeries and the requalification of patients for potentially curative interventions, outcomes that demonstrate the real-world impact of improved staging accuracy. In terms of treatment planning,

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PET-CT prompted alterations in clinical management in 35% of the cohort, including modifications in radiotherapy dose and field delineation based on metabolic tumor volume and response. This was particularly evident in NSCLC and HNSCC, where metabolic information refined gross tumor volume definition, enhancing the precision of radiotherapy. Furthermore, interim PET (iPET) using the Deauville scoring system allowed for chemotherapy de-escalation or intensification in lymphoma, supporting the shift towards risk-adapted regimens. In breast cancer, particularly triple-negative subtypes, early SUVmax reduction on PET-CT correlated with pathological complete response, mirroring findings from previous neoadjuvant chemotherapy trials (15). These response metrics served as robust surrogates for prognosis, enabling dynamic treatment modulation.

The prognostic capability of PET-CT was evident, with complete metabolic responders exhibiting significantly prolonged progression-free survival. Multivariate analysis confirmed that CMR and PMR were independent predictors of improved outcomes, echoing literature that positions metabolic response assessment as superior to conventional anatomic imaging in forecasting therapeutic success (16). Such evidence reinforces the inclusion of PET-derived parameters like SUVmax, MTV, and TLG in future clinical trials and practice guidelines. The diagnostic performance of PET-CT in detecting recurrence was also noteworthy, with high sensitivity and specificity, particularly in patients presenting with isolated tumor marker elevations and unremarkable conventional imaging. PET-CT enabled early detection of clinically actionable metastases, allowing timely and potentially curative interventions, notably in colorectal cancer cases with rising CEA levels. These findings support the growing role of PET-CT in longitudinal surveillance strategies within oncology care pathways (17). Integration of PET-CT within the broader framework of personalized oncology appears promising. Advances in radiomics and artificial intelligence are redefining the interpretative capacity of imaging data. The addition of texture-based radiomic features to traditional SUV metrics has shown promise in refining risk stratification in lymphoma and lung cancer (18). AI-driven tools now assist with automated lesion segmentation and prognostic modeling, although their clinical deployment awaits further validation (19). Beyond imaging, PET-CT also aligns well with theranostic strategies, exemplified by the dual diagnostic-therapeutic use of radiotracers such as 68Ga-PSMA and 177Lu-PSMA in prostate cancer, highlighting the convergence of diagnostics and therapeutics on a single platform (20). As imaging-genomics and liquid biopsy technologies mature, the role of PET-CT as a non-invasive biomarker hub is expected to expand, facilitating real-time treatment monitoring and resistance profiling.

Nevertheless, certain limitations should be acknowledged. The retrospective nature of the study introduced a potential selection bias, as patients referred for PET-CT may represent more complex clinical scenarios. The single-center design may limit the generalizability of results, particularly to institutions with differing imaging protocols or access to PET-CT infrastructure. Histopathological confirmation of PET-positive findings was not universally available, and thus the potential for false positives or negatives, especially in inflammatory or post-therapy contexts, cannot be excluded. Moreover, while progression-free survival was analyzed, overall survival data were limited due to heterogeneity in follow-up duration. Importantly, newer PET imaging modalities such as PET-MRI or immune PET were not included in this evaluation, and their role in enhancing diagnostic accuracy and tumor characterization remains an avenue for future investigation. Despite these constraints, the study provides a comprehensive and realistic reflection of how PET-CT is utilized in everyday oncologic practice. Its strength lies in its inclusive patient population, broad tumor representation, and detailed exploration of therapeutic consequences and survival outcomes associated with imaging findings. These characteristics contribute to the external validity and relevance of the results. The findings also highlight several directions for future work. Prospective multicenter studies are warranted to validate the predictive power of PET-derived biomarkers and radiomic signatures across diverse tumor types and patient demographics. Harmonization of imaging protocols and adoption of unified response criteria (e.g., PERCIST) will enhance comparability across clinical settings (21). The integration of AI algorithms for automated analysis, real-time decision-making, and outcome prediction holds substantial promise and demands prospective evaluation (22). Furthermore, the convergence of PET imaging with genomic and proteomic data could yield novel imaging-genomic biomarkers, enabling therapy selection and resistance prediction in a minimally invasive manner (23). Expansion of radiotracer development, including those targeting immune checkpoints, tumor microenvironment, and amino acid metabolism, will extend the utility of PET-CT to previously non-avid tumors and broaden its diagnostic and therapeutic scope (24). Attention should also be paid to ensuring equitable access to PET-CT, especially in low-resource settings, through cost-effectiveness studies and scalable implementation strategies. In conclusion, this study substantiates the transformative role of PET-CT in modern oncology. It is no longer confined to diagnostic use but is actively shaping therapeutic pathways, improving risk stratification, and supporting precision-guided interventions. With continued innovation and integration, PET-CT stands as a cornerstone in the shift toward truly personalized cancer care.

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CONCLUSION

This study concludes that PET-CT fusion imaging holds a pivotal role in the advancement of personalized oncology by offering a comprehensive view of tumor biology through the integration of functional and anatomical data. Its influence spans the entire continuum of cancer care—from initial diagnosis and staging to real-time response assessment and long-term surveillance. The findings reinforce PET-CT's ability to modify staging, guide therapeutic decisions, and predict patient outcomes, underscoring its value as both a diagnostic and prognostic tool. The use of specialized radiotracers has extended its reach to tumor types previously challenging to assess, while the integration of radiomics and AI is unlocking new dimensions in personalized treatment planning and risk prediction. Despite its underutilization in resource-limited settings, efforts to expand accessibility and standardize imaging protocols are underway. Overall, this research affirms PET-CT as a cornerstone of modern oncology, with the potential to transform clinical decision-making and enable more precise, individualized cancer care.

AUTHOR CONTRIBUTION

Author	Contribution
Sadhu Ram Raika*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Mukesh Kumar	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Govind Ram	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Harchand Rabari	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Erum Dangrach	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Mahwish Pirzado	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published
Avesh Kumar	Contributed to study concept and Data collection Has given Final Approval of the version to be published

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