RESEARCH PAPER

Role of 18F-FDG PET/CT and triphasic computed tomography in evaluation of patients with malignant hepatic focal lesions undergoing thermal ablation as local treatment response

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ABSTRACT

Background: Hepatocellular carcinoma (HCC) and liver metastases pose significant diagnostic challenges, particularly regarding early detection of extra-hepatic disease and monitoring post-treatment changes. This prospective study compares the diagnostic performance and prognostic utility of 18F-FDG PET/CT versus contrast-enhanced triple-phase computed tomography (CECT) in patients undergoing radiofrequency ablation (RFA) or trans-arterial chemoembolization (TACE).

Methods: Eighty-eight patients with laboratory and radiologically confirmed primary HCC or secondary liver metastases were prospectively enrolled. Baseline and sequential follow-up tracking via 18F-FDG PET/CT and CECT were performed to assess extra-hepatic staging, local recurrence, and volumetric/metabolic tumor response parameters in correlation with therapy response and 24-month overall survival (OS).

Results: For patients managed with RFA, 18F-FDG PET/CT demonstrated superior diagnostic accuracy for extra-hepatic staging compared to CECT (sensitivity 100% vs. 60%; accuracy 97.78% vs. 79.1%). Similarly, in the TACE cohort, 18F-FDG PET/CT vastly outperformed CECT, which suffered from a high false-positive rate and low sensitivity (PET/CT accuracy 97.78% vs. CECT 68.8%). While no baseline parameters significantly impacted therapy response and survival in the RFA group, baseline tumor size and Total Lesion Glycolysis (TLG) showed a significant moderate negative correlation with 24-month OS in the TACE cohort ($P<0.05$).

Conclusion: Functional 18F-FDG PET/CT provides significantly superior diagnostic accuracy for extra-hepatic metastasis mapping compared to conventional CECT. Furthermore, metabolic parameters like TLG hold vital prognostic value for stratifying overall survival in advanced-stage cohorts undergoing TACE.

Keywords: 18F-FDG PET/CT; radiofrequency ablation; early response; extra-hepatic metastases; overall survival; hepatic malignancy.

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INTRODUCTION

Primary liver cancer remains the sixth most commonly diagnosed cancer and the third leading cause of cancer-related mortality globally (1). Within Egypt, liver cancer ranks first in national incidence, prevalence, and mortality creating a severe clinical burden (2). Furthermore, secondary metastatic liver tumors are even more prevalent than primary malignancies, presenting a continuous clinical challenge in oncology management. (3)(4).

While loco-regional therapeutic strategies such as radiofrequency ablation (RFA) and trans-arterial chemoembolization (TACE) are standard-of-care treatments to induce tumor necrosis, structural imaging response criteria (e.g., RECIST, WHO) often fall short (5). Post-treatment changes, regional thermal inflammation, and altered perfusion dynamics complicate the morphological differentiation between residual viable tumor and therapeutic necrosis on conventional Computed Tomography (CT) or Magnetic Resonance Imaging (MRI) (6)(7).

Functional molecular imaging using 18F-fluorodeoxyglucose (18F-FDG PET/CT) bypasses structural limitations by assessing cellular glucose metabolic changes (8) (9). While the sensitivity of 18F-FDG for highly differentiated primary HCC varies, it's utility in detecting early extra-hepatic metastasis—crucial for tailoring clinical interventions—remains robust.

This prospective study aims to evaluate the diagnostic accuracy of baseline 18F-FDG PET/CT versus conventional CT in identifying extra-hepatic disease, and to characterize whether PET/CT-derived semi-quantitative and volumetric metabolic parameters act as reliable predictors of therapy response and overall survival (OS) in patients undergoing local ablative or trans-catheter therapies.

2. Methods

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2.1 Study Population

This prospective study was approved by the Institutional Ethical Committee of the National Cancer Institute (NCI), Egypt. Over the period from August 2021 to December 2023, 88 patients (59 males, 29 females; mean age 59 +/- 12 years) presenting with confirmed malignant hepatic focal lesions were enrolled.

- **Inclusion Criteria:** Patients aged >16 years old with laboratory, histo-pathologically, and/or radiologically verified primary hepatic carcinoma or liver metastases, scheduled for RFA or TACE, with no major macrovascular invasion.
- **Exclusion Criteria:** Patients with contrast allergies, pregnancy, blood glucose levels exceeding 180 mg/dl at the time of tracking, lesions <10mm, or severe underlying hepato-renal impairment.

2.2 Imaging Protocols

- **Triple-Phase Contrast-Enhanced CT (CECT):** CT scans were acquired using a dual-source 64-slice system. Biphasic/triphasic imaging captures were meticulously timed: hepatic arterial phase (25–30 s delay), portal venous phase (65–70 s delay), and delayed interstitial phase (150–200 s delay) using 2 ml/kg of non-ionic iodinated contrast media. Scan intervals between PET and CECT were restricted within a maximum of 2 weeks.
- **18F-FDG PET/CT Procedure:** Patients fasted for a minimum of 6 hours, ensuring a blood glucose level <160 mg/dl before receiving an intravenous weight-adjusted dose of FDG} (1mCi/10 kg). Following a 60-minute resting bio-distribution period, three-dimensional whole-body scanning was executed without repositioning the patient.

2.3 Image Interpretation and Reference Standards

Images were independently evaluated by two experienced nuclear medicine physicians blinded to clinical timelines. In cases of mismatch, a final consensus reading was utilized.

1. **CT Evaluation:** Response evaluation incorporated functional changes via mRECIST and LI-RADS treatment response algorithms (TRA) to track viable arterially enhancing components versus treatment-induced necrosis.
2. **PET/CT Evaluation:** Evaluated qualitatively (focal uptake exceeding healthy liver background) and semi-quantitatively using maximum standardized uptake value (SUVmax), SUVmean, metabolic tumor volume (MTV), and total lesion glycolysis (TLG).
3. **Reference Standard:** Diagnosis of true extra-hepatic disease and local tumor progression (LTP) was established via serial imaging (6–12 months progression), clinical/biochemical tumor marker tracking (AFP dynamics), or guided histological biopsies where clinically feasible.

2.4 Statistical Analysis

All data management was completed via IBM SPSS Version 28. Numerical variables were checked for parametric normality using Kolmogorov-Smirnov and Shapiro-Wilk testing. Comparative analytics utilized non-parametric Mann-Whitney and Wilcoxon tests. Diagnostic metrics (sensitivity, specificity, PPV, NPV, and accuracy) were computed. Correlation strengths were mapped via Spearman's rank correlation coefficient (r). Kaplan-Meier survival evaluations and univariate log-rank parameters were tracked at the 24-month clinical endpoint.

3. Results

3.1 Patient and Tumor Characteristics

Of the 88 included patients, 77 (87.5%) were diagnosed with HCC, while 11 (12.5%) presented with metastatic liver lesions (63.6% from colorectal cancer primary sites). Segmental liver involvement showed 61 patients (69.3%) with single-segment disease and 27 patients (30.7%) with multi-segment disease. The baseline primary target tumor size ranged between 1.0 to 22.0 cm, with an average mean size of 6.0cm – **(Table 1).**

Table (1): Socio-demographic characteristics of study's participants of 88 patients with cancer liver	**n=88(%)**
Age (Mean ±SD)	**59 ±12**
Sex	
Female	**29 (33%)**
Male	**59 (67%)**
HCC or Mets	
Hepatocellular carcinoma	**77 (87.5%)**
Metastatic Cancer liver	**11 (12.2%)**
Tumor size (Cm)	**Mean Size: 6 cm (1-22)**
Site (Segment)	
Multiple segment	**27 (30.7%)**
Single Segment	**61 (69.3%)**

3.2 Extra-Hepatic Metastasis Staging Performance

Pronounced differences emerged when mapping out extra-hepatic disease before local intervention:

- **Radiofrequency Ablation Cohort (43 patients):** 18F-FDG PET/CT correctly mapped distant metastases with a sensitivity of 100%, specificity of 92.86%, and an overall accuracy of 97.78%. Conversely, routine CECT produced 3 false positives and missed metastases in 3 active cases, dropping its sensitivity to 60.0% and overall accuracy to 79.1% ($P < 0.001$) **(Table 2).**

Table (2): Sensitivity, Specificity, PPV, NPV and accuracy of PET/CT vs CT in detection of extra-hepatic metastases in patients managed by RFA.

PET/CT		Conventional CT	
Sensitivity	100.00%	Sensitivity	60.00%
Specificity	92.8%	Specificity	91.8%
Positive Predictive Value	96.8%	Positive Predictive Value	50.00%
Negative Predictive Value	100%	Negative Predictive Value	89.1%
Accuracy	97.8%	Accuracy	79.1%

- **Trans-Arterial Chemoembolization Cohort (45 patients):** 18F-FDG PET/CT verified true extra-hepatic lesions in nearly 71% of TACE candidates with a sensitivity of 100% and an overall diagnostic accuracy of 97.78%. Conventional structural CECT missed metastatic sites in 17 active cases and yielded 10 false-positive assessments, culminating in a drastically reduced sensitivity of 77.7%, specificity of 62.9%, and overall accuracy of 68.8% **(Table 3).**

Table (3): Sensitivity, Specificity, PPV, NPV and accuracy of PET/CT vs CT in detection of extra-hepatic metastases in patients managed by RFA.

PET/CT		Conventional CT	
Sensitivity	100.00%	Sensitivity	77.70%
Specificity	92.8%	Specificity	62.9%
Positive Predictive Value	96.8%	Positive Predictive Value	58.3%
Negative Predictive Value	100%	Negative Predictive Value	80.9%
Accuracy	97.8%	Accuracy	68.8%

3.3 Prognostic Value of Volumetric and Metabolic Parameters on therapy response and Survival

- **RFA Treatment Arm:** Mean overall survival at 24 months reached 80% across the RFA sub-cohort. However, baseline primary tumor sizes and metabolic variables SUVmax, SUVmean, MTV, and TLG demonstrated no statistically significant correlation with therapy response and 24-month survival endpoints ($P > 0.05$).

In RFA patients: at 24-months, we found that mean overall survival to be 80% **(Fig 1).**

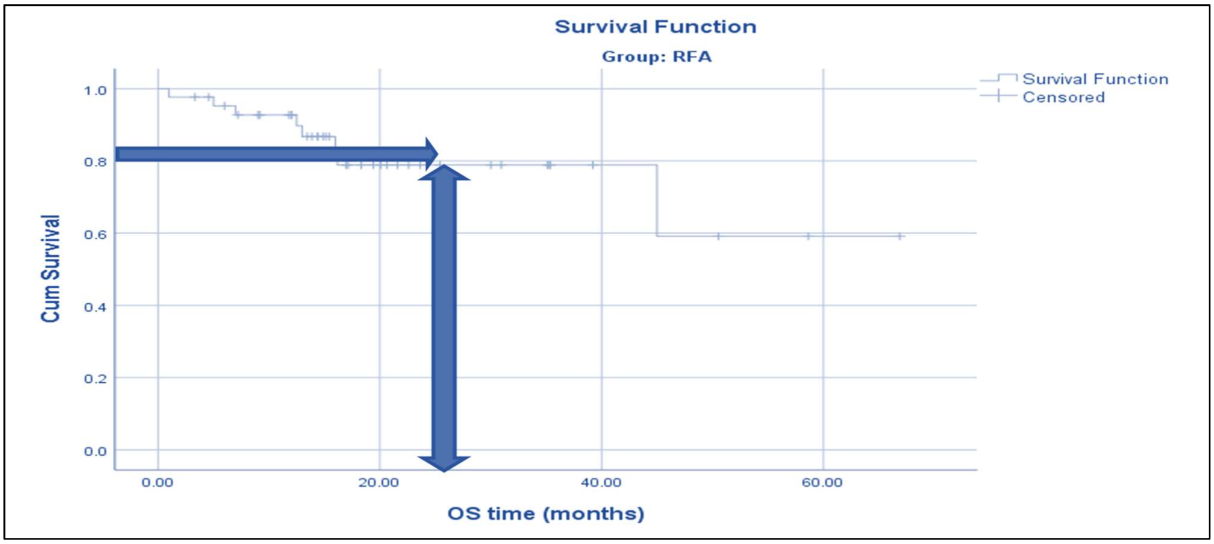

Figure 1. The patient has been diagnosed with HCC. Figure 1a is pre-ablation revealed segment II FDG avid focal lesion. Figure 1b same day post ablation showed a hypometabolic, hypodense hepatic area (segment II), consistent with a well-ablated hepatic lesion

- **TACE Treatment Arm:** The advanced TACE arm demonstrated a lower 24-month survival rate of approximately 30%. Statistical analysis revealed a distinct, moderate inverse correlation between overall survival times and both initial tumor size (r = -0.359) and Total Lesion Glycolysis (TLG) (r = -0.299). Higher baseline sizes and greater metabolic glycolytic tumor burden directly corresponded to shorter overall survival timelines ($P < 0.05$).

In TACE patients: at 24-months, the mean overall survival was 30% **(Fig 3).**

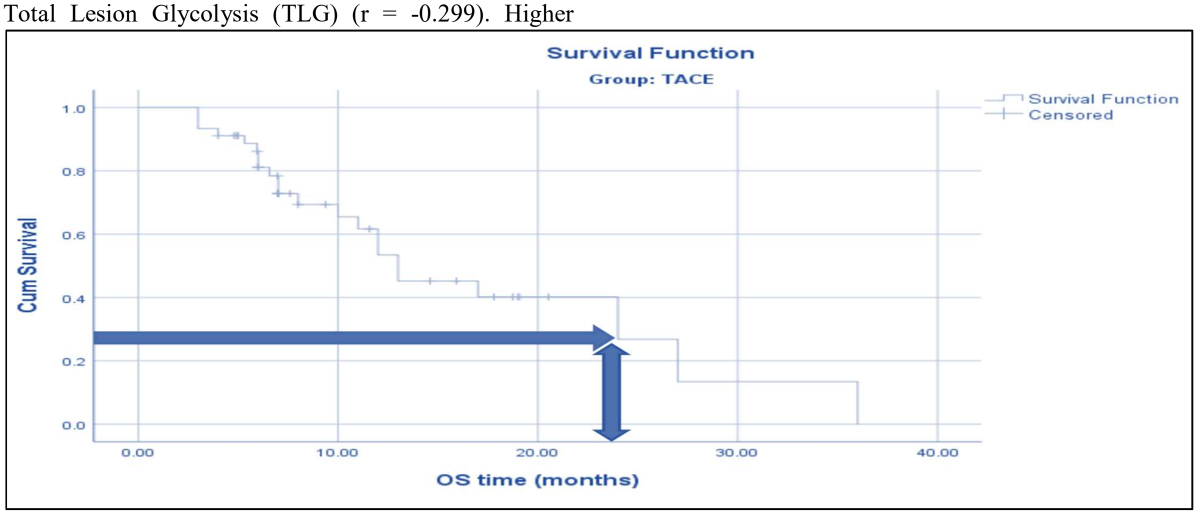

Figure 2. The patient was diagnosed with metastatic colon adenocarcinoma to liver. The same-day post-ablation PET sca n revealed a segment VIII hypometabolic non-FDG avid hepatic focal area, with its periphery displaying nodular FDG ac tivity consistent with residual viable tumor tissue

4. Discussion

Choosing an optimal management path for malignant liver lesions requires precise initial staging and accurate differentiation of post-treatment tissue responses. This prospective investigation demonstrates that metabolic imaging via 18F-FDG PET/CT offers a significantly higher diagnostic capability compared to structural triple-phase CECT for defining extra-hepatic disease before therapeutic local interventions.

Our findings align with international data. Studies such as those **by Kuehl et al. (2008)** and **Georgakopoulos et al. (2013)** highlighted that functional PET/CT detection alterations change clinical workflows in 25–26% of intended RFA candidates by revealing occult extra-hepatic lesions missed on standard morphologic scans (10)(11). Our investigation underscores the superior diagnostic capability of 18F-FDG PET/CT over conventional CT in mapping extra-hepatic disease. For patients undergoing RFA, functional PET/CT significantly outperformed morphology-based CT across all diagnostic parameters, notably achieving a higher overall accuracy **(97.7% vs. 79.1%)** and eliminating false-negative findings

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(sensitivity: 100% vs. 60.0%). This diagnostic superiority persisted within the advanced TACE cohort, where PET/CT achieved an overall accuracy of 97.7% compared to the suboptimal 68.8% demonstrated by conventional CT. These findings strongly align with data reported **by Elmenshawy et al. (2020),** who similarly concluded that 18F-FDG PET/CT offers enhanced accuracy in identifying occult extra-hepatic metastases—a pivotal factor in optimizing patient staging and subsequent therapeutic management decisions (12).

Regarding prognostication, our findings differentiate the utility of metabolic tracking across treatment modes. For the RFA cohort, baseline metabolic or size criteria lacked statistical weight regarding therapy response and 24-month survival metrics. This can be attributed to the curative intent of ablation tailored for localized tumor volumes.

In contrast, in the advanced TACE therapeutic subgroup, initial tumor size and Total Lesion Glycolysis (TLG) displayed significant negative correlations with overall survival. TLG combines both volumetric parameters and metabolic activity, offering a more comprehensive assessment of total metabolic tumor burden compared to simple standard uptake values SUVmax alone. Integrating advanced metabolic data allows clinicians to identify patients with high tumor burdens who may experience early progression, enabling a personalized transition toward systemic therapies.

Study Limitations: This study was conducted at a single oncology reference powerhouse (NCI, Egypt) and included a mixed cohort of primary HCC and diverse secondary liver metastases. Future multi-center investigations focusing on isolated cell types are recommended to validate optimal cutoff criteria for volumetric metabolic tumor metrics.

Conclusion: 18F-FDG PET/CT provides superior accuracy for extra-hepatic metastasis mapping compared to conventional CT in patients with malignant liver lesions scheduled for loco-regional therapy. For patients undergoing TACE, baseline tumor size and TLG serve as valuable independent prognostic markers to help guide clinical management.

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