ONLINE ISSN :3007-309X
PRINT ISSN :3007-3081

Journal of Medical & Health Sciences Review

# DUAL-TRACER PET/CT IMAGING IN THYROID CARCINOMA: COMPLEMENTARY ROLES OF $^{18}$F-FDG AND $^{68}$GA-DOTATATE IN DETECTING RECURRENCE AND METASTASIS

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**ARTICLE INFO**

**Keywords:** Thyroid Cancer, Carcinoma, Positron Emission Tomography, Diagnosis, Computed Tomography.

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**ABSTRACT**

**Background:** Thyroid carcinoma is a highly aggressive tumor, often giving rise to recurrent cancer and metastatic cancer even after the surgical treatment. Early detection of thyroid cancer is essential for improving long term treatment and patient survival rate.

**Objective:** To compare the diagnostic accuracy of PET/ CT with the conventional methods and radioactive iodine scans in the management of thyroid cancer.

**Methodology:** Published reports of comparing the diagnostic accuracy of PET/ CT with the conventional methods and radioactive iodine scans in the management of thyroid cancer were identified by a systematic search of Google Scholar, PubMed, Research Gate, Springer and the Sci Hub, supplemented with citation tracking. From 1001 initially identified studies, only 13 studies met the inclusion criteria after screening and duplicate removal. These studies compared the diagnostic accuracy of PET/ CT with the conventional methods and radioactive iodine scans in the management of thyroid cancer, using standard statistical measures, typically at a 95% confidence level.

**Results:** The literature reviewed reveals that PET/CT imaging, especially when using 18F-FDG, is important in managing thyroid cancer especially when the

conventional imaging tools such as radioactive iodine (RAI) scans and ultrasound fail to clearly indicate the condition. PET/CT has a good diagnostic accuracy in the diagnosis of recurrent or metastatic disease in patients with Thyroglobulin-Elevated Negative Iodine Scintigraphy (TENIS) with spilling sensitivity and specificity to 94.3 percent and 78.4 percent, respectively. It has better sensitivity in detecting metastases that are at a distance particularly that of poorly differentiated and anaplastic thyroid carcinomas where there is reduced avidity to iodine and standard scans are ineffective. Although RAI whole-body scanning is still useful as an initial stage diagnostic procedure and in detection of remnants in differentiated thyroid cancers (DTCs), PET/CT has added accuracy in localizing metabolically active disease especially in follow-up of postoperative patient or in biochemical recurrence when RAI scans are negative. Moreover, it has been seen that 18F-FDOPA PET/CT is more sensitive in enlightening the recurrence of medullary thyroid carcinoma (MTC), particularly in those cases where the level of calcitonin is high in the patients. In general, PET/CT is adding value to the existing imaging protocol because of yielding metabolic information contributing to better staging and planning of the treatment decisions and ultimately in enhancing the overall results of the patient in aggressive/biochemically active thyroid cancers, which do not demonstrate well on conventional modalities.

**Conclusion:** PET/CT scanning exhibits high sensitivity and specificity values in the diagnosis of local recurrence and metastases in post- surgical patients with medullary thyroid carcinoma. Furthermore, based on a comparative analysis of18F-FDG and GA68-DOTATE, it appears that these radiotracers are particularly sensitive and reliable for highlighting MTC, and it was found that there were no statistical differences in terms of sensitivity and specificity. Therefore, these two modalities appear to be complementary in monitoring MTC patients.

## INTRODUCTION:

Computed Tomography (CT) and Positron Emission Tomography/Computed Tomography (PET/CT) have become best imaging modalities in the management of thyroid cancer, particularly in conditions where traditional imaging modalities may fall short. While ultrasound and radioactive iodine (RAI) scans used as an initial evaluating methods, however PET/CT offers enhanced diagnostic applications in specific clinical scenarios. (1) Positron Emission Tomography combined with Computed Tomography (PET/CT), particularly using ^18F-

fluorodeoxyglucose (18F-FDG), has emerged as a pivotal imaging modality in the management of thyroid cancer. Its utility is especially pronounced in cases where traditional imaging techniques, such as radioactive iodine (RAI) scans, yield inconclusive results. (8) Follow-up in patients with differential thyroid cancer generally involves measurements of Thyroglobulin (Tg), Tg antibodies (Tg-Ab) and neck ultrasound. The conventional imaging methods used to differentiate thyroid cancer includes Computed Tomography CT and Magnetic Resonance Imaging (MRI) , for better anatomical information of the thyroid tissue as well as the neighboring structures. (2) In cases, where patients present with elevated serum thyroglobulin levels but negative iodine scans—a condition known as TENIS (Thyroglobulin-Elevated Negative Iodine Scintigraphy)—PET/CT becomes a valuable diagnostic tool. 18F-FDG PET/CT has demonstrated high sensitivity and specificity in detecting recurrent or metastatic disease in such scenarios. A meta-analysis reported pooled sensitivity and specificity rates of 94.3% and 78.4%, respectively, for FDG PET/CT in identifying recurrent DTC. (9) Whole-body scan (WBS) with radioiodine (131I) is the most effective method for tumor detection, staging, and treatment planning [1]. Iodine-131-WBS is useful for the differentiating tumors on the basis of its avidity to iodine, identifying remnant thyroid tissue, and evaluating distant metastatic disease. (2) Most well-differentiated thyroid carcinomas are relatively slow growing and can be FDG negative [3]. Therefore, the role of FDG PET/CT in the management of patients with DTC is primarily limited to postoperative follow-up. Because only 4–7% of patients with DTC present initially with distant metastasis, the routine use of an initial staging PET would not be indicated (9) Although, FDG PET does not provide information beyond that yielded by ultrasound for local preoperative assessment of thyroid cancer (7) several studies have reported that it has a high sensitivity (up to 85%) and specificity (up to 95%) for distant metastases in patients with DTC (5,6) Medullary thyroid carcinoma (MTC), arising from perifollicular C cells, often necessitates different imaging approaches due to its unique biological behavior. While 18F-FDG PET/CT can detect MTC lesions, its sensitivity is variable. Emerging evidence suggests that 18F-FDOPA PET/CT offers superior sensitivity and specificity in identifying recurrent or metastatic MTC, particularly in patients with elevated calcitonin levels in post-surgical conditions. (6) Anaplastic thyroid carcinoma (ATC) and poorly differentiated thyroid cancers are aggressive subtypes with limited treatment options. These tumors often exhibit high glucose metabolism, making 18F-FDG PET/CT particularly effective in their evaluation. PET/CT not only aids in accurate staging by

detecting distant metastases but also assists in assessing treatment response and guiding therapeutic decisions. (6,4,7) PET/CT is best diagnostic modality used to evaluate metastatic diseases in patients with differential thyroid carcinoma, presenting with a history of elevated uteroglobin levels but negative RAI scans. PET/CT localize the exact sore of disease that may not be possible through conventional imaging methods, thereby reduced times and enhanced diagnostic applications. (3) PET/CT plays a crucial role in staging and assessing the extent of disease spread such as poorly differentiated thyroid carcinomas. These subtypes often exhibit reduced iodine uptake, rendering RAI scans less effective, whereas PET/CT can identify metabolically active lesions. (4,5,6) In addition, DTC encompassing papillary and follicular subtypes, generally exhibits favorable outcomes with standard treatments like surgery and radioactive iodine therapy. (8)

**MATERIALS AND METHODS:**

**STUDY DESIGN:** This study is a systematic review of multiple articles that were published till the month of May, 2025 that compares the diagnostic accuracy of PET/ CT with the conventional methods and radioactive iodine scans in the management of thyroid cancer. This study is reported in accordance with PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines as shown in figure 1.

**SEARCH STRATEGY:** Published reports that compared the diagnostic accuracy of PET/ CT with the conventional methods and radioactive iodine scans in the management of thyroid cancer were identified by a systematic search of Google Scholar, PubMed, ResearchGate, Science direct, Springer and the Sci Hub, supplemented with citation tracking. The search was made using combinations of the following keywords: “Thyroid cancer”, “Carcinoma”, “Positron emission tomography” and “Computed tomography”. In addition, BOOLEAN operators such as “AND” and “OR” were used for efficient search strategy.

**INCLUSION AND EXCLUSION CRITERIA:** Publications published till May 2025 were included in our study. From 1001 initially identified studies, 13 studies met the inclusion criteria after screening and duplicate removal. The studies included original articles, reviews and meta-analysis that consisted of at least one of the following terms: “PET”, “Thyroid Carcinoma”, “diagnosis of thyroid cancer” . The inclusion criteria included full text articles exclusively presented in English language.

The exclusion criteria consisted of conference abstracts, publications in languages other than English or without English translation and studies that did not mark a clear comparison between the diagnostic efficiency of PET/CT and conventional imaging modalities in the diagnosis and follow-up of thyroid carcinomas.

**RESULTS:** The search strategy generated 1001 publications.988 studies were excluded as they did not meet the selection criteria. These studies were related to other imaging modalities, other types of cancers or comparison between the diagnostic accuracy of imaging modalities other than PET/CT and conventional imaging modalities for thyroid cancer. A total of 13 studies were included and subjected to the comparative quality assessment of imaging technologies in the detection and diagnosis of thyroid cancer. The references to these studies are numbered and added to this paper in the references. 599 studies were published in a language other than English and therefore, were excluded from the study. The literature reviewed reveals that PET/CT imaging, especially when using 18F-FDG, is important in managing thyroid cancer especially when the conventional imaging tools such as radioactive iodine (RAI) scans and ultrasound fail to clearly indicate the condition. PET/CT has a good diagnostic accuracy in the diagnosis of recurrent or metastatic disease in patients with Thyroglobulin-Elevated Negative Iodine Scintigraphy (TENIS) with spilling sensitivity and specificity to 94.3 percent and 78.4 percent, respectively. It has better sensitivity in detecting metastases that are at a distance particularly that of poorly differentiated and anaplastic thyroid carcinomas where there is reduced avidity to iodine and standard scans are ineffective. Although RAI whole-body scanning is still useful as an initial stage diagnostic procedure and in detection of remnants in differentiated thyroid cancers (DTCs), PET/CT has added accuracy in localizing metabolically active disease especially in follow-up of postoperative patient or in biochemical recurrence when RAI scans are negative. Moreover, it has been seen that 18F-FDOPA PET/CT is more sensitive in enlightening the recurrence of medullary thyroid carcinoma (MTC), particularly in those cases where the level of calcitonin is high in the patients. In general, PET/CT is adding value to the existing imaging protocol because of yielding metabolic information contributing to better staging and planning of the treatment decisions and ultimately in enhancing the overall results of the patient in aggressive/biochemically active thyroid cancers, which do not demonstrate well on conventional modalities.

| Imaging Modality | Sensitivity | Specificity | Key Findings |
|---|---|---|---|
| **18F-FDG PET/CT** | 94.3% | 78.4% | High sensitivity for recurrent DTC in TENIS cases |
| **18F-FDG PET/CT** | Up to 85% | Up to 95% | Superior for distant metastases in DTC |
| **18F-FDOPA PET/CT** | Higher than FDG | Higher than FDG | Best for recurrent/metastatic MTC (high calcitonin) |
| **18F-FDG PET/CT** | Very High | High | Anaplastic/Poorly Differentiated TC (glucose-avid) |
| **I-131 WBS (RAI)** | High (iodine-avid tumors) | High | Best for **initial staging** in DTC |
| **Ultrasound vs. PET** | Lower than PET | Comparable | PET better for distant mets, US for local assessment |

**DISCUSSION:**

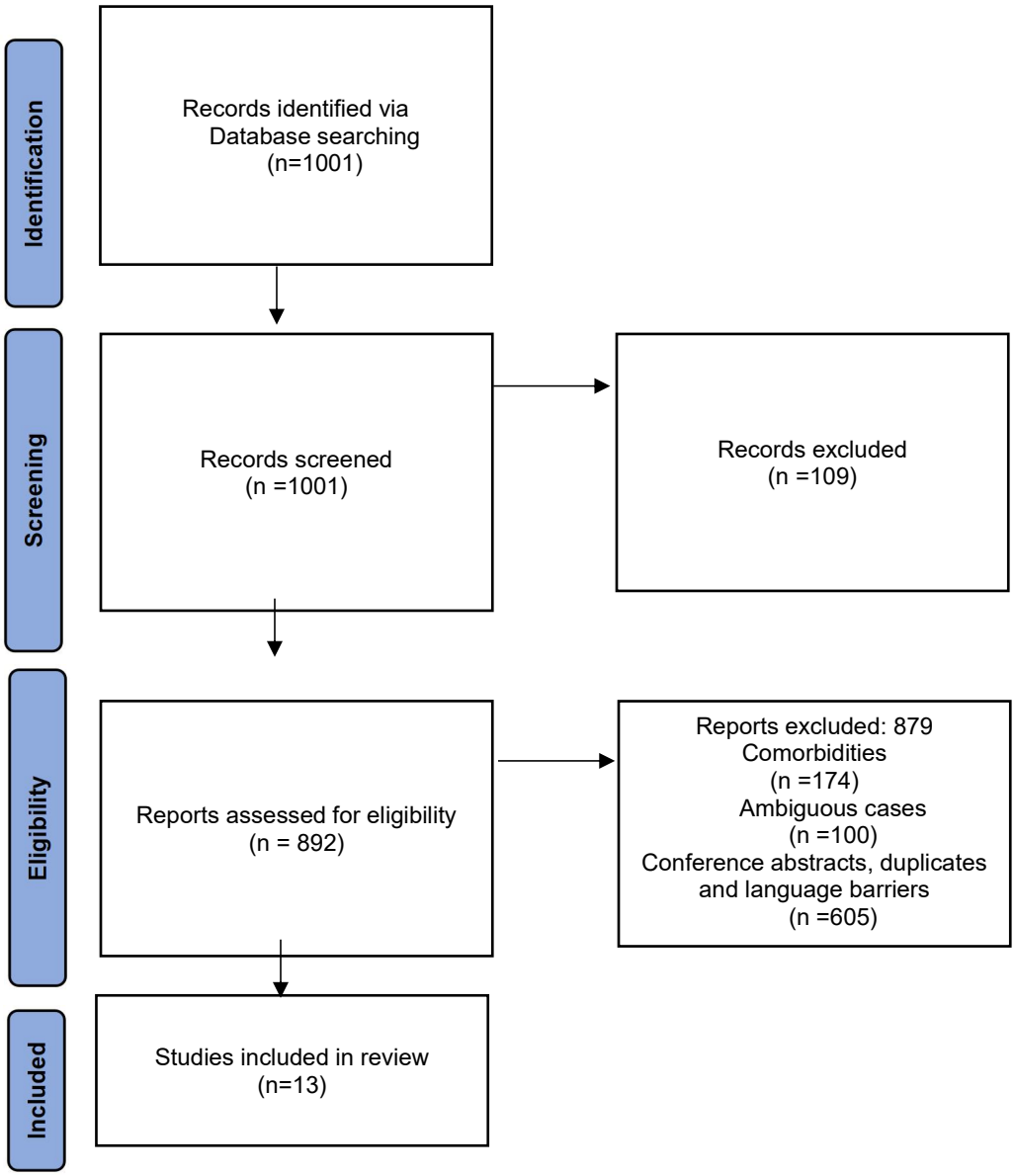
The literature evidence is very high in favoring the emerging role of the PET/CT, especially with 18F-FDG, as a promising imaging modality in the detection and diagnosis of thyroid cancers, especially when the classic methods of the RAI scintigraphy and the ultrasound are not an option. PET/CT has a higher sensitivity level (94.3%) with a reasonable specificity level (78.4%) in the identification of recurrent or metastatic disease in TENIS patients, where conventional iodine-based scans have not identified the pathology even when the levels of thyroglobulin are high. Notably, PET/CT shows increased efficacy in establishing remote metastases, especially in undifferentiated and anaplastic thyroid carcinoma due to low iodine contents, RAI-imaging becomes largely ineffective in these cases. Although, RAI whole-body scanning remains relevant in the early screening and follow-up of differentiated thyroid cancers (DTCs), PET/CT plays an important role in post-surgery follow-up and biochemical recurrence offering metabolic

information that is not present in conventional techniques. Also, 18F-FDOPA PET/CT in medullary thyroid carcinoma (MTC) shows good future development and using 18F-FDOPA PET/CT has a higher sensitivity in patients with high calcitonin level who experience recurrence of the disease. In general, PET/ CT adds to the current procedures, providing functional imaging information which allows more specific restaging, treatment planning, and prognostic evaluation mainly in aggressive or biochemically active thyroid malignancy. The adoption of it for regular follow-up, particularly in high-risk groups, or unusual presentations, would have the potential to improve the decision-making of clinicians and, finally, patient outcomes as well.

**CONLUSION:**

This systematic review shows that PET/CT scanning exhibits high sensitivity and specificity values in the diagnosis of local recurrence and metastases in post- surgical patients with medullary thyroid carcinoma. Furthermore, based on a comparative analysis of18F-FDG and GA68-DOTATE, it appears that these radiotracers are particularly sensitive and reliable for highlighting MTC, and it was found that there were no statistical differences in terms of sensitivity and specificity. Therefore, these two modalities appear to be complementary in monitoring MTC patients.

**FIGURE 1: PRISMA Flow chart**

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