

فَإِنَّ لِلَّذِينَ ظَلَمُوا
عِندَ رَبِّهِمْ فِي الْحَمِيَّةِ
عَذَابًا
وَهُمْ فِيهَا
يُكَلِّمُونَ

Clinical Indication of FDG PET-CT in DTC

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Current PET Radiotracers in Iran

- ^{18}F FDG : Breast, Lymphoma, Lung, GI , GU, Iodine Refractory DTC, HEAD & NECK, Melanoma
- ^{68}Ga -Dotatate: NETs
- ^{68}Ga -PSMA : Prostate Cancer

^{18}F FDG PET-CT

- The role of FDG PET-CT in oncology is rapidly expanding in clinical practice worldwide.
- Valuable clinical tool for the detection, staging, and management of several malignant tumors.

Value of FDG-PET/CT

- Evaluate specific metabolic pathways.
- Combine metabolic images provided by PET with anatomic images obtained by CT (greater specificity and accuracy than either PET or CT alone).

^{18}F FDG PET-CT

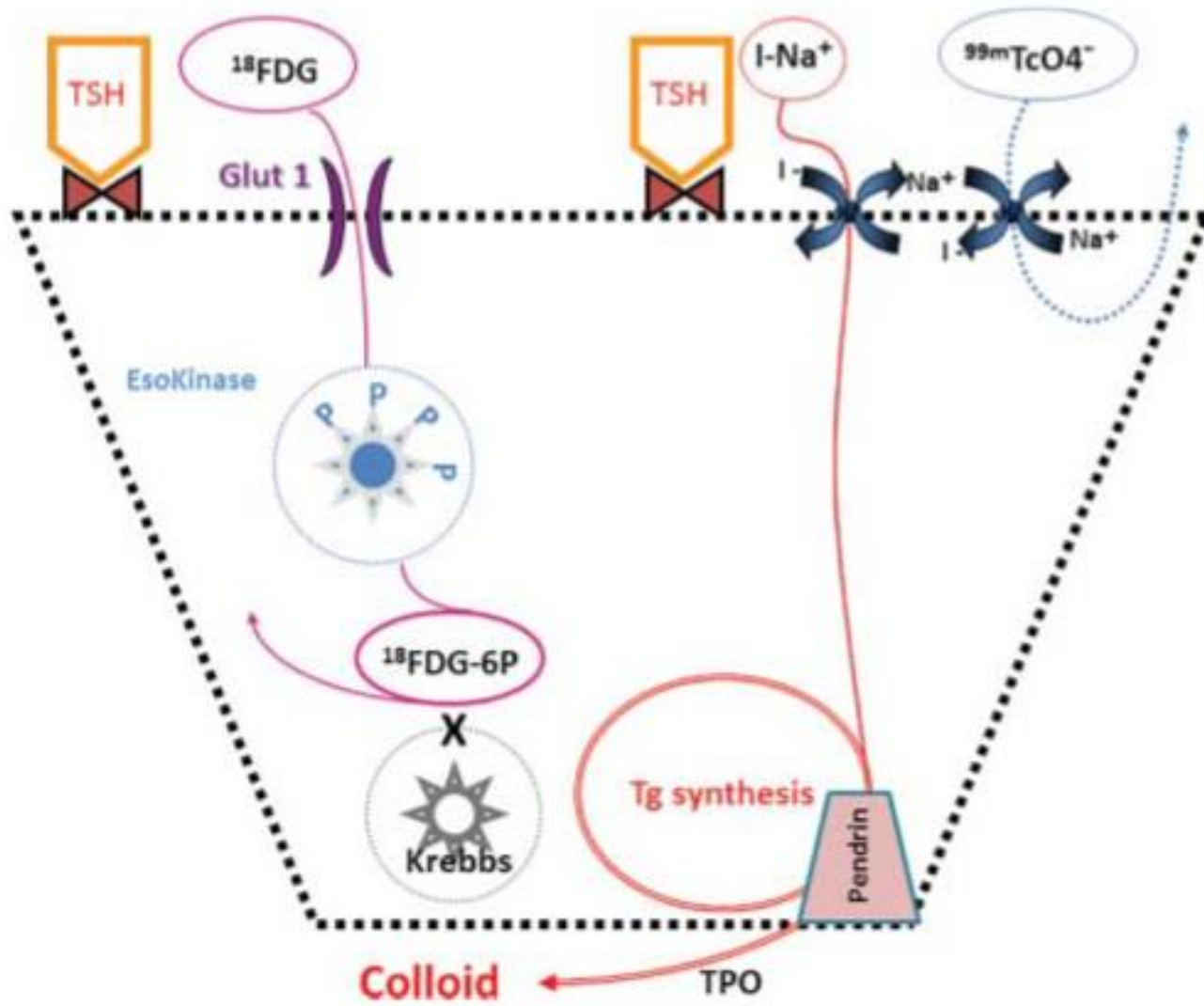
lymphoma, melanoma, Breast cancer and metastatic gastro-intestinal,
lung, head and neck cancer, GU

^{18}F FDG PET-CT

In thyroid tumors, however, an increased uptake of FDG is restricted to more aggressive and high-grade tumors, and no significant tracer uptake occurs in well-differentiated tumors .

^{18}F FDG PET-CT

In 1996, Feine et al. reported an inverse relationship between RAI and FDG uptake in thyroid carcinoma (the so-called 'flip-flop phenomenon').



^{18}F FDG PET-CT

- **FDG uptake** is not unique to cancer cells and can also occur in such benign cells as **macrophages and granulocytes**, which are present in the foci of **infection and inflammation** .

Clinical Indication of FDG PET-CT in DTC

- Defined Indication
- Not completely defined Indication

Clinical Indication of FDG PET-CT in DTC

Defined Indication :

- In patients with elevated thyroglobulin levels but negative cervical ultrasound study and radioiodine whole-body scan
- As a tool of prognostic significance

Clinical Indication of FDG PET-CT in DTC

Not completely defined Indication:

- In patients with radioiodine refractory disease
- To evaluate the response to molecular-targeted therapies
- In the initial staging and follow-up of patients with aggressive histological subtypes.
- In thyroid nodules with indeterminate fine-needle aspiration cytology.
- For radio-guided surgery

Defined indications

1-Elevated Tg levels but negative neck ultrasound and radioiodine WBS

- After initial treatment, 20% of patients have Tg elevation but negative WBS, and these cases represent a major diagnostic challenge.
- In 25% of cases, the Tg level decreases spontaneously over months to years (18 months) after the initial treatment without additional therapy, which underlines the importance of re-stratification and dynamic risk assessment.

Defined indications

1-Elevated Tg levels but negative neck ultrasound and radioiodine WBS

- A rising unstimulated or stimulated serum Tg over time will typically identify patients that have a residual disease that is likely to become clinically apparent.
- In these patients, neck ultrasound (US) is highly sensitive in the detection of cervical metastases, and it can also guide fine-needle aspiration for cytology (FNAC) and identify Tg in needle washout fluid.

1-Elevated Tg levels but negative neck ultrasound and radioiodine WBS

- Cases of detectable Tg levels and negative neck US are common in daily practice.
- These patients are usually evaluated by means of MRI, CT, and WBS 2–5 mCi.
- However, the role of Dx WBS has been questioned because this technique is rarely able to localize disease .

Defined indications

1-Elevated Tg levels but negative neck ultrasound and radioiodine WBS

If no disease sites are identified by chest CT or DxWBS,

FDG-PET/CT or empiric RAI therapy followed by WBS (TxWBS) should be performed to identify recurrent or metastatic disease.

Defined indications

1-Elevated Tg levels but negative neck ultrasound and radioiodine WBS

- FDG PET-CT Sensitivity and specificity values of 88.5 and 84.7% respectively.
- Tg cutoff value, clinical characteristics, histological subtype and by TSH stimulation.

Defined indications

1-Elevated Tg levels but negative neck US and radioiodine WBS

False-negative Pet-CT :

- Negligible accumulation of FDG, especially near regions of physiological FDG uptake (e.g., palatine tonsils, soft palate, lingual tonsils, and tongue) .
- Small tumors that are below the spatial resolution of PET.
- Well-differentiated thyroid tumors often exhibit inherently low rates of glycolysis and result in a low FDG uptake .

Defined indications

1-Elevated Tg levels but negative neck US and radioiodine WBS

False positive FDG PET-CT:

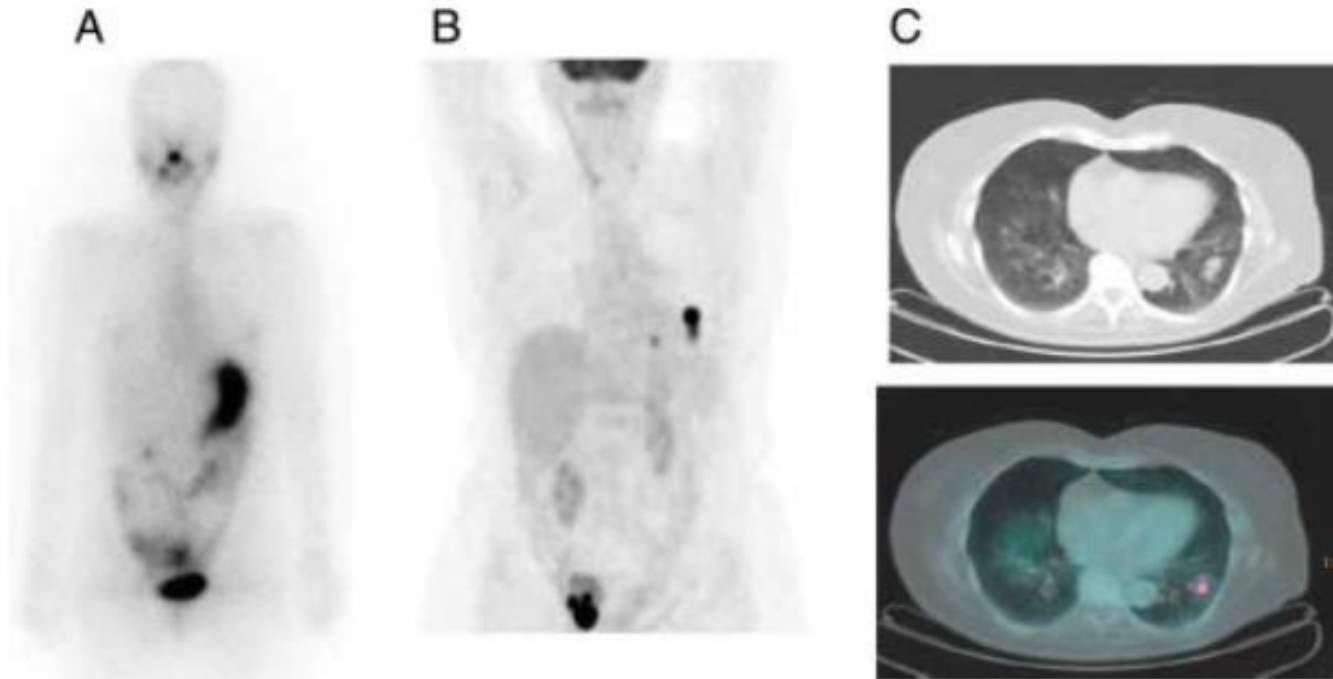
- Inflammatory lymph nodes.
- Suture granulomas.
- Increased nonspecific muscle uptake of FDG

Histologic confirmation may be required before one can be certain that an FDG-positive lesion represents metastatic disease.

Defined indications

1-Elevated Tg levels but negative neck US and radioiodine WBS

Empirical RAI therapy be used only in patients with negative or not significant FDG uptake.



Negative radioiodine anterior whole-body scan in a 37-year-old male patient with elevated serum Tg levels, (23 ng/ml).

(B,C) FDG-PET/CT scan showing a focus of increased tracer uptake in the left lung that corresponds to a lung metastasis.

Defined indications

1-Elevated Tg levels but negative neck US and radioiodine WBS

- Leboulleux et al. evaluated the sensitivity of TxWBS vs FDG-PET/CT in 23 DTC patients with elevated serum Tg levels.
- The sensitivities for the detection of individual lesions were 88% for FDG-PET/CT and 16 % for TxWBS .
- FDG-PET/CT was abnormal in 22 patients, five of whom also had an abnormal TxWBS. Only one patient had an abnormal TxWBS and a normal FDG-PET/C.
- The authors concluded that in patients with suspected recurrence based on the Tg level after a first normal TxWBS, FDG-PET/CT, rather than a second TxWBS, should be used to localize the disease.

Defined indications

1-Elevated Tg levels but negative neck US and radioiodine WBS

Positive PET/CT findings in patients with elevated Tg levels but negative WBS may also change patient management in 20–40% of cases .

Defined indications

1-Elevated Tg levels but negative neck US and radioiodine WBS

FDG PET-CT management changes :

- Initiation or avoidance of surgical procedures.
- Further work-up with imaging studies or biopsies.
- Initiation and guidance of external beam radiotherapy.
- Conversion from treatment with a curative intent to palliative management in the setting of advanced disease

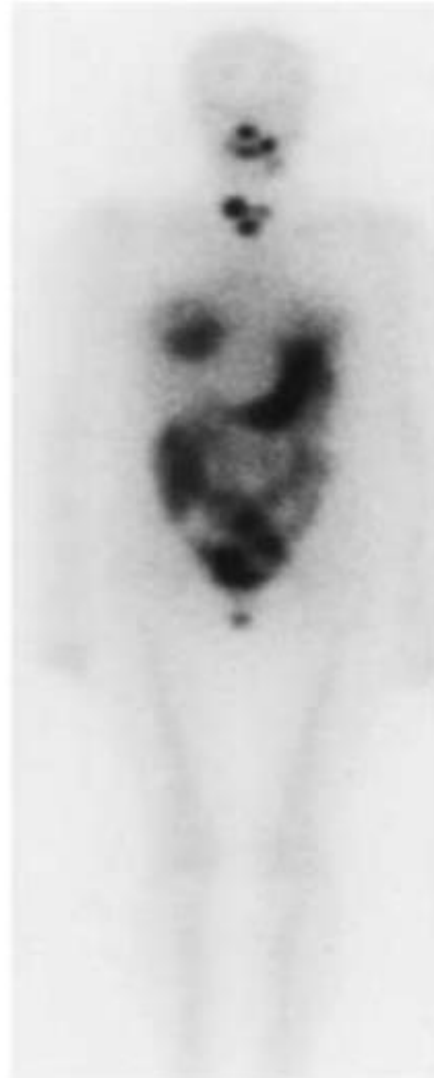
Cost Effective?

Defined Indication

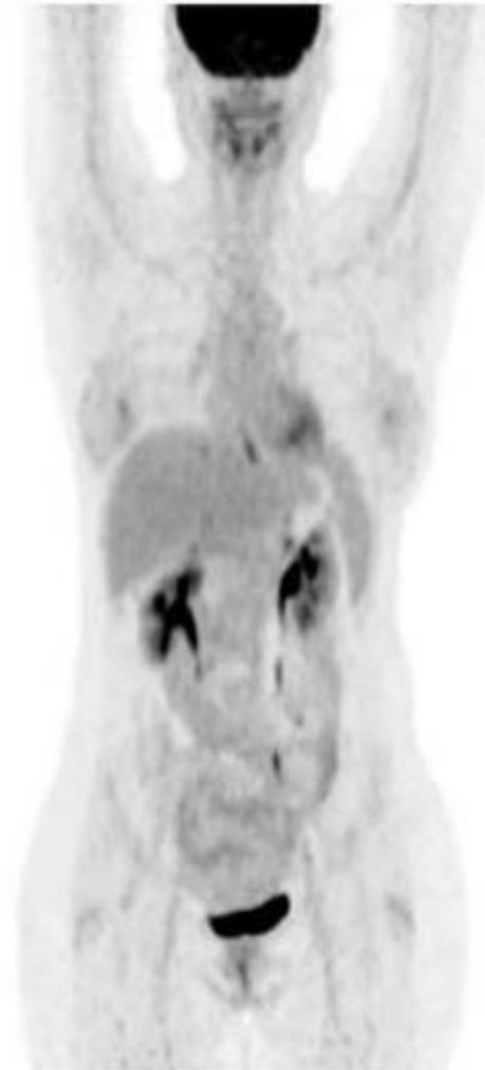
2-As a tool of prognostic significance

- Metastatic DTC who have high FDG uptake, which suggests more dedifferentiated, aggressive, and metabolically active tumor cells and thereby indicates poorer prognosis and reduced survival.
- Negative FDG-PET/CT predicts a more favorable prognosis in patients that have a positive RAI scan.

A



B



Radioiodine anterior whole-body scan (A)

and FDG-PET scan (B)

in a 48-year-old female patient submitted to total thyroidectomy and radioiodine therapy for lymph node and

lung metastases. Note the intense radioiodine uptake, which corresponds to lung and lymph node metastases, and the absence of FDG uptake.

Defined Indication

2-As a tool of prognostic significance

High volume (>125 ml) of FDG-avid disease provided stronger prognostic information than age, sex, initial histological type or grade, RAI uptake.

Defined Indication

2-As a tool of prognostic significance


- Vuralet al evaluated the prognostic significance of negative FDG-PET/CT scans in DTC patients with negative WBS and elevated stimulated Tg levels that could be suppressed by hormone therapy.
- No recurrence was detected in PET-negative patients with undetectable/suppressible Tg levels on levothyroxine therapy.
- The authors hypothesized that these patients were affected by metastatic cancer that was suppressible by keeping TSH levels very low
- Although the source of the serum Tg might also have been related to nonfunctioning or very poorly functioning thyroglossal tract tissue that was not visualized by WBS but was able to synthesize Tg.

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ORIGINAL ARTICLES

Prognostic Significance of FDG PET/CT on the Follow-Up of Patients of Differentiated Thyroid Carcinoma With Negative ^{131}I Whole-Body Scan and Elevated Thyroglobulin Levels

Correlation With Clinical and Histopathologic Characteristics and Long-Term Follow-Up Data

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Not yet completely defined indications

1-Patients with radioiodine refractory disease

- Two-thirds of metastatic patients show substantial RAI uptake.
- Complete remission is achieved in more than two-thirds of patients with recurrent lymph node disease and in only one-third of patients with distant metastases .

Not yet completely defined indications

1-Patients with radioiodine refractory disease

RAI refractory DTC :

- Metastatic disease that does not take up RAI at the time of initial treatment
- Tumors lose the ability to take up RAI after previous evidence of uptake .
- RAI uptake retained in some lesions but not in others .
- Metastatic disease that progresses despite substantial uptake of RAI

Not yet completely defined indications

1-Patients with radioiodine refractory disease

Neck US, CT scan of the neck, chest, and abdomen, and MRI of the brain, spine, and pelvis.

FDG-PET/CT should be used both to complete the staging and to assess the disease progression rate .

Not yet completely defined indications

1-Patients with radioiodine refractory disease

FDG-PET/CT can help identify patients who need surgery, external radiation therapy, radiofrequency ablation, cryotherapy, cement injection, or embolization.

These treatment modalities could permit a physician to postpone the onset of a systemic treatment.

Not yet completely defined indications

2-To evaluate the response to molecular-targeted therapies (TKIs)

- The use of TKIs should be limited to a highly selected group of metastatic patients, because their toxicities are numerous, frequently serious, and occasionally fatal .
- FDG-PET/CT can provide a basis for more uniform patient selection than traditional selection criteria, such as evidence of disease progression by changes in tumor size .
- In addition, by detecting metabolic changes within the tumor, FDGPET/CT may enable early assessment of the effect of treatment (7 days after treatment!!!).

Not yet completely defined indications

3-In the initial staging and follow-up of high-risk patients with aggressive histological subtypes

- Aggressive histologic subtypes of thyroid carcinoma, namely Hurthle cell carcinoma (HCTC), poorly differentiated thyroid carcinoma, and anaplastic thyroid carcinoma (ATC).
- These tumors usually do not concentrate significant amounts of RAI and have a worse prognosis than that of well-differentiated thyroid carcinomas.
- FDG-PET/CT could improve disease staging and thereby potentially change the clinical management of patients.



FDG-PET/CT scan in a 45-year-old male patient
Hurthle cell thyroid carcinoma.
High metabolic activity in two latero-cervical lymph nodes.
Tg levels of 47.5 ng/ml - negative whole body scan

Not yet completely defined indications

4-In thyroid nodules with indeterminate fine-needle aspiration cytology

- The studies have variable and sometimes conflicting results.
- American Thyroid Association guidelines recommend neither for nor against the use of FDG-PET .
- High sensitivity but low specificity.

Not yet completely defined indications

5-FDG-PET/CT and 18F-FDG for radioguided surgery

18F-FDG can be used during radioguided surgery (RGS) to identify cervical recurrence of RAI-negative DTC using a handheld gamma probe

Controversies

1-Cutoff value of Tg for the selection of patients for FDG-PET/CT

- According to the ATA guidelines , FDG-PET/CT should be performed only when unstimulated Tg levels exceed 10 ng/ml.
- Insurance Providers
- PET or PET-CT
- TG DT <1 year
- Although serum Tg levels correlate with tumor load and true-positive FDG-PET/CT scans increase as Tg levels increase, several authors have suggested FDG-PET in Tg level < 10 can detect some patients.

Controversies

2-FDG-PET/CT scanning with TSH stimulation

- TSH stimulates the glucose transport system by enhancing the number GLUT transporters in the plasma by stimulating the glycolytic pathway

- TSH stimulation (T4 withdrawal or rhTSH administration) significantly improves the sensitivity of FDG-PET/CT and that TSH stimulation should be recommended for DTC patients who are undergoing PET scanning for elevated Tg levels and iodine-negative scanning.

- Thyrogen?, Corticosteroide therapy?

Controversies

2-FDG-PET/CT scanning with TSH stimulation

According to the ATA guidelines,

the sensitivity of FDGPET/CT scanning may be marginally improved with TSH stimulation (especially in patients with low Tg values), but the clinical benefit of identifying these additional small foci has yet to be proven.

Controversies

3-Clinical significance of thyroid PET Incidentaloma

Thyroid incidentaloma diagnosed by FDG-PET/CT is defined as thyroid FDG uptake incidentally and newly detected in a patient who is being studied for a nonthyroid purpose.

Increasing FGD PET-CT  Increased Incidentaloma

Controversies

3-Clinical significance of thyroid PET Incidentaloma

Most are benign

Some Malignancy most PTC

Secondary lesion from other tumors.

- Focal FDG uptake → Risk of malignancy
- Diffuse FGD uptake → acute or chronic thyroiditis.

Table 2 Main recommendations of international thyroid societies for the use of FDG-PET in thyroid cancer.

	BTA	ATA	NCCN	LATS	ESMO	ETA
Preoperative use		No		Aggressive cancers	Undifferentiated thyroid cancers	No
Elevated Tg and negative WBS	Tg on LT4 ≥ 10 ng/ml; rising Tg on LT4	Tg on LT4 ≥ 10 ng/ml	Tg on LT4 ≥ 10 ng/ml; TSH-Tg $> 2-5$ ng/ml	Tg on LT4 ≥ 10 ng/ml	Tg on LT4 ≥ 10 ng/ml; rising Tg on LT4	Tg on LT4 ≥ 10 ng/ml; TSH-Tg $> 2-5$ ng/ml
High-risk patients and aggressive histology		High-risk DTC; poor DTC; invasive Hürthle cell carcinoma; after systemic or local therapy of metastases	Poor DTC; invasive Hürthle cell carcinoma			pT4 tumors; poor DTC; invasive HCC; before aggressive therapy

BTA, British Thyroid Association; ATA, American Thyroid Association; NCCN, National Comprehensive Cancer Network; LATS, Latin American Thyroid Society; ESMO, European Society for Medical Oncology; ETA, European Thyroid Association; DTC, differentiated thyroid cancer; Tg, thyroglobulin; WBS, whole-body scan.

Thank You

