INCIDENTAL THYROID UPTAKE ON PET SCANNING

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INTRODUCTION

- Incidental lesions of the thyroid are increasingly discovered as the prevalence of medical imaging escalates.
- Most forms of diagnostic imaging showed a growth rate of 2- to 6-fold between 2000 and 2016 in both the United States and Canada, a trend expected worldwide.
- Imaging studies may be performed for a multitude of reasons, such as screening, staging, or surveillance of cancerous and noncancerous diagnoses.
- While studies may be undertaken for a specific and targeted purpose, the possibility of unveiling incidental lesions cannot be ignored.
- The likelihood of revealing an incidental finding varies substantially (< 5% to 22%) depending on the chosen imaging modality. (Whole body imaging more).

INTRODUCTION

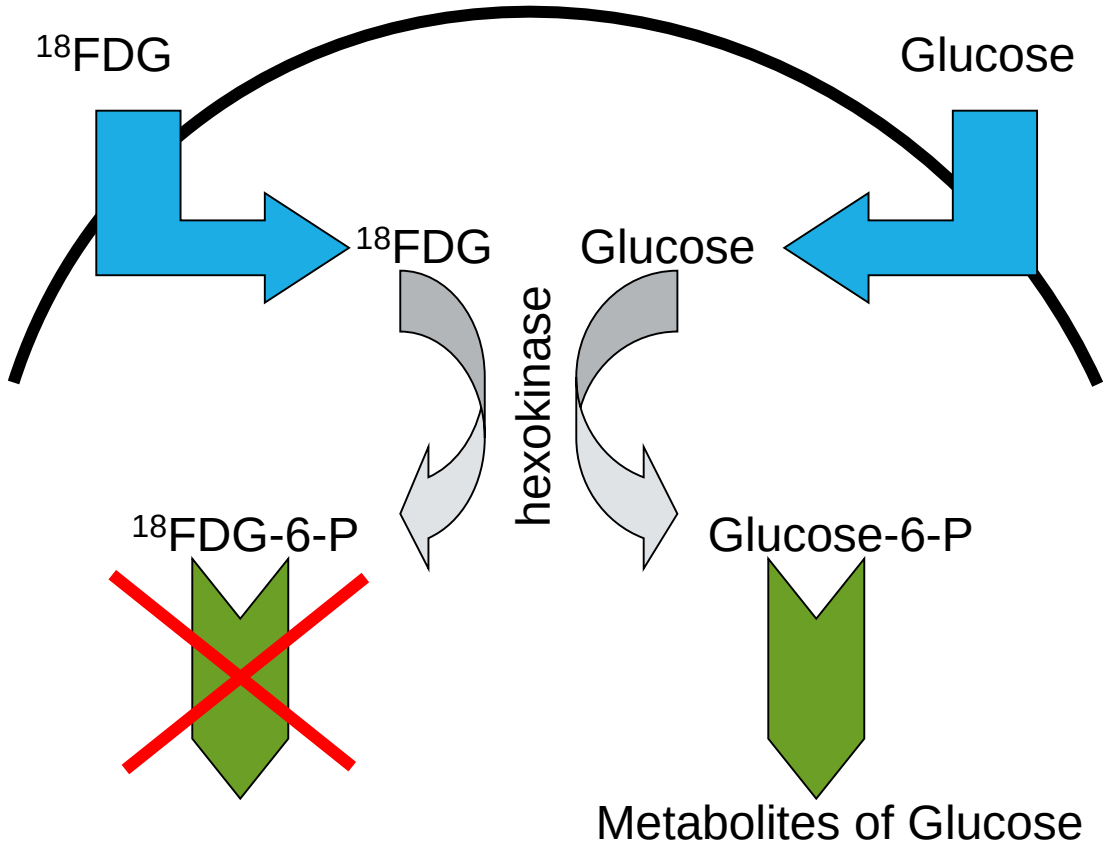
- The primary concern of an incidentally discovered lesion, commonly termed an *incidentaloma*, relates to the associated risk of malignancy.(metastasis, metachoronus versus synchronous to first cancer).
- Thyroiditis? , Thyroid function abnormalities?

- While all imaging modalities may unveil incidentalomas, the metabolic data afforded by functional imaging such as ^{18}F-FDG PET/CT may provide further information to decipher the clinical relevance of such lesions.
- Anatomic versus functional imaging

INTRODUCTION

- ^{18}F-FDG is a glucose analog that shows uptake levels corresponding to glycolysis rates and glucose consumption.
- It is frequently elevated in cancerous tissues due to inefficient aerobic glycolysis (termed the Warburg effect).
- Physiologic FDG uptake is reported in brown fat, skeletal muscle, lymphoid tissue, and the thymus.
- Multiple benign etiologies, primarily inflammatory or infectious in origin, may also exhibit uptake due to increased rates of glucose metabolism.

GENERAL ASPECTS(^{18}FDG)



INTRODUCTION

- Second primary malignancies were described in 4.1%-8.5% of PET/CT scans completed for staging or surveillance purposes.
- Interestingly, some studies describe a higher likelihood of incidentalomas in patients undergoing PET/CT for screening purposes (3.0%-3.1%) compared to the evaluation of known or suspected cancer (1.9%-2.3%).
- 2 million PET/CT scans performed annually in the United States, these small fractions add up to a significant number of lesions that must be addressed. (Iran ?)

INTRODUCTION

- Incidentally discovered lesions in the thyroid are uncovered in 21%-34% of neck ultrasound examinations and 16% of CT or MRI scans.
- Among these lesions, the risk of malignancy is reported to range from 1.5%-11%.

INTRODUCTION

- On PET scans, the thyroid gland exhibits very low physiologic FDG avidity.
- Oncocytic/Hürthle cell lesions (both benign and malignant) are known to exhibit FDG-avidity due to an intrinsic mitochondrial defect that results in inefficient glycolytic metabolism.
- Thyroid malignancies, such as papillary, follicular, and anaplastic carcinomas and thyroid lymphoma, may also be expected to exhibit increased FDG uptake due to increased glucose metabolism.

INTRODUCTION

- Incidental FDG-avid uptake in the thyroid gland exists in two predominant patterns : focal and diffuse.
- The overall detection rate of thyroid incidentalomas on PET/CT, irrespective of uptake patterns, is estimated at 1.5%-4.2%.
- Most reports attribute a risk of malignancy of 5.1%-22.0% of these PET-detected thyroid incidentalomas notably higher than those detected by ultrasound or CT (1.5-11%).

PATTERNS OF FDG UPTAKE IN THE THYROID GLAND

- Within the thyroid, FDG uptake has been described in focal and diffuse patterns or combinations.
- In general, lesions are designated as focal when the focus of uptake comprises less than one lobe of the thyroid, although such lesions may be multifocal and thus occur bilaterally.
- The term diffuse is applied when homogenous uptake is identified.
- Diffuse-plus-focal uptake has been described as focal lesions overlying a background of diffuse uptake.

- Table describes the incidence of thyroid incidentalomas noted in selected references along with the absolute numbers of malignancies diagnosed.
- Unfortunately, it is impossible to determine the true rate of malignancy in this population as a significant proportion of patients do not undergo further investigation due to their underlying disease status.

Table 1. Incidence and malignancy in PET-detected thyroid incidentalomas

Authors	Country	#PET/CT scans	Incidence				Malignancy		
			Cumulative	Focal	Diffuse	Diffuse + focal	Focal	Diffuse	Diffuse + focal
Ceriani *et al.*[25]	Switzerland	12,652	333 (2.6%)	187 (1.5%)	146 (1.2%)	-	30	-	-
Beck *et al.*[40]	USA	35,124	-	227 (0.6%)	-	-	59	-	-
Kim *et al.*[41]	Korea	39,098*	-	-	635 (1.6%)	-	-	-	-
Gedberg *et al.*[26]	Denmark	2451	-	59 (2.4%)	-	-	10	-	-
Pattison *et al.*[32]	Australia	45,680	-	500 (1.1%)	-	-	-	-	-
Ozderya *et al.*[42]	Turkey	6873	138 (2.0%)	135 (2.0%)	3 (0.04%)	-	27	-	-
Makis *et al.*[43]	Canada	7252	-	157 (2.2%)	-	-	14	-	-
Sencan Eren *et al.*[35]†	Turkey	4204	178 (4.2%)	68 (1.6%)	35 (0.8%)	13 (0.3%)	11	-	4
Kim *et al.*[24]	Korea	18,172	-	358 (2.0%)	-	-	51	-	-
Chun *et al.*[29]	Korea	2584	-	52 (2.0%)	-	-	15	-	-
Jamsek *et al.*[36]	Slovenia	5911	230 (3.9%)	148 (2.5%)	82 (1.4%)	-	10	-	-
Brindle *et al.*[33]	UK	7221	156 (2.2%)	81 (1.1%)	75 (1.0%)	-	7	1	-
Lee *et al.*[30]	Korea	2368	-	64 (2.7%)	-	-	11	-	-
Nishimori *et al.*[18]	Canada	6457	160 (2.5%)	103 (1.6%)	57 (0.9%)	-	9	0	-
Kang *et al.*[44]	Korea	12,840*	1151 (9.0%)	612 (4.8%)	539 (4.2%)	-	55	2	-
Chen *et al.*[45]	USA	2594	99 (3.8%)	53 (2.0%)	46 (1.8%)	-	7	0	-
Karantanis *et al.*[34]	USA	4732	-	-	138 (2.9%)	-	-	0	-
Kurata *et al.*[46]	Japan	1626	-	-	25 (1.5%)	4 (0.24%)	-	1	2
Choi *et al.*[16]	Korea	1763	-	65 (3.7%)	-	5 (0.28%)	18	-	0
Nockel *et al.*[47]† DOTATATE	USA	237	26 (11.0%)	14 (5.9%)	12 (5.1%)	-	3	0	-

#Number of PET/CT scans. *Study population included PET/CT scans completed for screening/preventative measures. †Prospective study.

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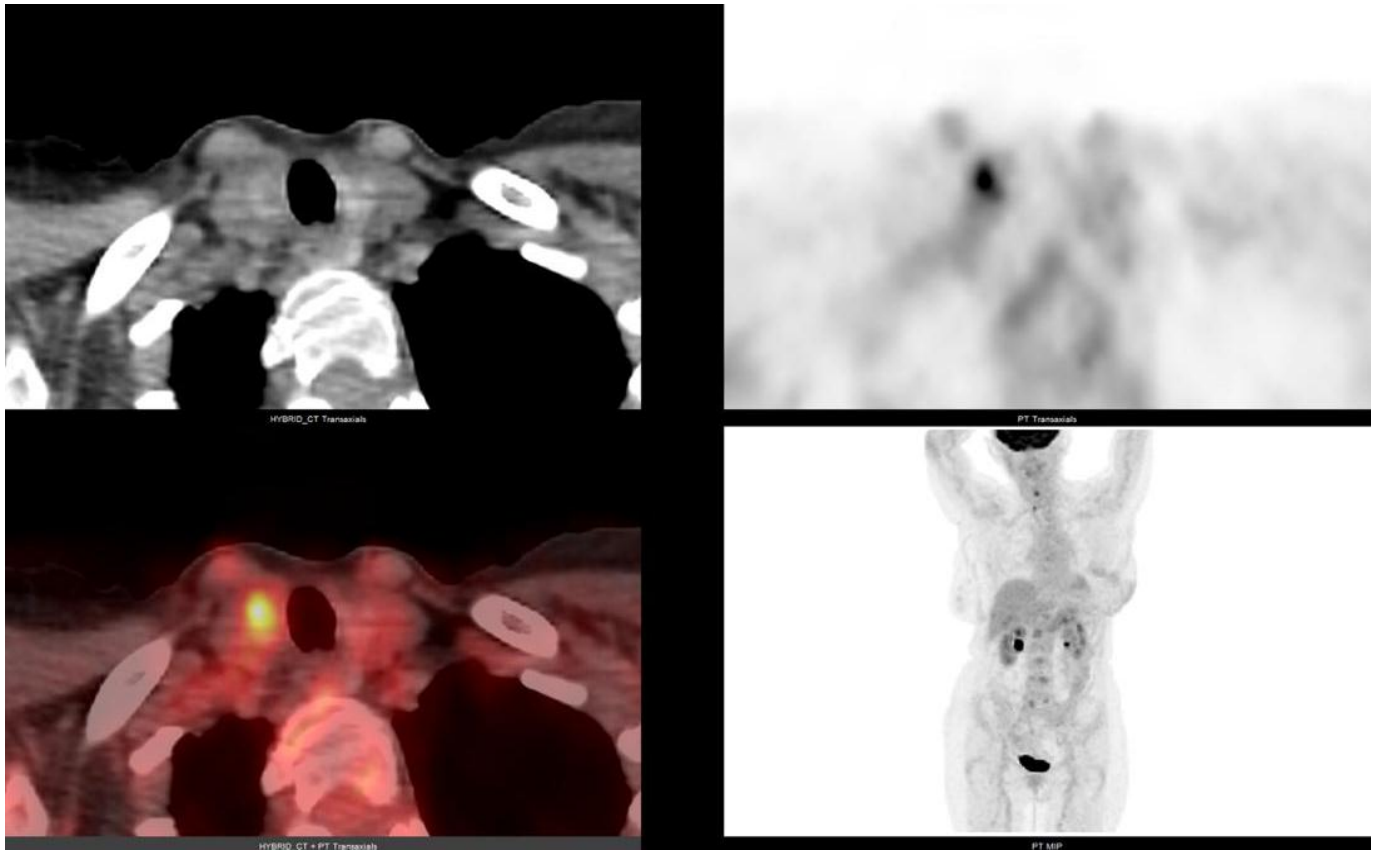
FOCAL FDG UPTAKE



This is a case of focal thyroid FDG uptake in a 79-year-old female who underwent PET scanning for known laryngeal cancer.
This revealed a 1.1 cm thyroid lesion in the right lower thyroid pole, SUV 6.0.

PATTERNS OF FDG UPTAKE IN THE THYROID GLAND

- Focal thyroid uptake is defined as FDG avidity occurring in less than one lobe of the thyroid gland for which we suggested the term PEToma .
- The prevalence of such lesions is reported in approximately 0.5%- 2.5% of PET/CT imaging studies.
- Most of studies describe a slightly higher rate of detection of focal *vs*. diffuse patterns of uptake.
- The malignancy risk amongst the focal lesions seems to be much greater, with rates ranging from 8.6%-50%.
- In Asian countries, the rate of focal uptake has been reported to be double that of American studies, yet the rate of cancer is unchanged.

PATTERNS OF FDG UPTAKE IN THE THYROID GLAND

- A retrospective study of 4726 patients (6457 FDG PET/CT scans) revealed a 3.4% rate of thyroid incidentalomas (160 of 6457 PET/CT scans).
- Focal uptake was noted in 2.2% (103 patients), and uptake was diffuse in 1.2% (57 patients).
- Fifty patients with focal uptake underwent further workup with imaging and/or fine-needle aspiration and cytology (FNAC), and thyroidectomy was completed in 10 patients.
- Nine of the ten surgical patients were ultimately diagnosed with papillary thyroid carcinoma on final histopathology: two micropapillary carcinomas, two extrathyroidal extensions, four multifocal involvement, and one had > 50% poorly differentiated papillary thyroid carcinoma.
- Thirty percent of the PETomas that received a tissue diagnosis (FNAC and/or histology) were cancerous, which relates to 8.7% of all focal thyroid lesions.

DIFFUSE FDG UPTAKE

This is a case of mild diffuse FDG uptake throughout the thyroid with SUV 3.7 in a patient undergoing PET scanning for known metastatic sarcoma.

DIFFUSE FDG UPTAKE

- Diffuse FDG uptake is reported in most studies at slightly lower rates than focal uptake.

- Yasuda *et al*. (Japan 2 decades ago) investigated 1102 healthy subjects using the 18F-FDG PET scan, and they detected diffuse FDG thyroidal uptake in 36 (3.26%), only one of whom was found to have hypothyroidism.

- Furthermore, antithyroid antibodies were positive in 27 subjects, which led these authors to conclude that diffuse thyroidal FDG uptake may be an indicator of chronic thyroiditis.

DIFFUSE FDG UPTAKE

- In a review of eight studies, the frequency of diffuse FDG uptake ranged from 0.1%-4.5%, with a mean of 1.9%.

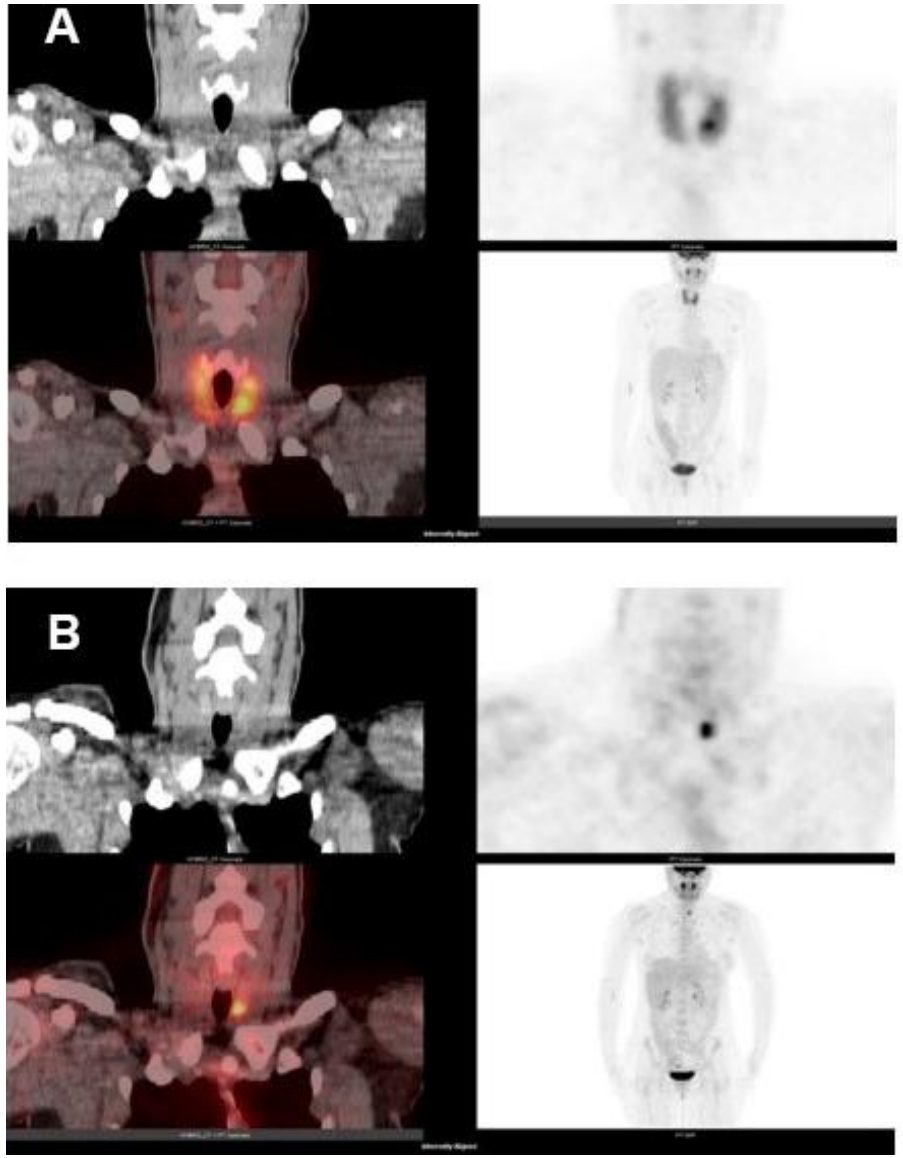
- Contemporary studies similar to Yasuda *et al* namely that the diffuse uptake pattern is an indication of benign disease, predominantly attributed to inflammatory or autoimmune forms of thyroiditis such as Hashimoto's thyroiditis.

- Only 10% of patients with these conditions exhibit diffuse FDG uptake on PET scan.

DIFFUSE FDG UPTAKE

- There is no apparent relationship between serum TSH levels and diffuse FDG avidity in patients diagnosed with thyroiditis.
- Thyroid hormone replacement seems to have no effect on patterns of uptake.
- Impact of incidentally identified diffuse uptake on subsequent thyroid dysfunction was unclear.
- Kim *et al* euthyroid patients identified with diffuse thyroid uptake on PET scan should be regarded as being at risk for future development of thyroid dysfunction and should be followed up.
- Risk of malignancy in diffuse thyroidal uptake on FDG-PET scan is very low.

DIFFUSE-PLUS-FOCAL FDG UPTAKE



This is a case of diffuse-plus-focal FDG uptake transitioned to focal uptake in a patient with Stage III melanoma.
Final pathology after total thyroidectomy showed multifocal papillary thyroid carcinoma.

DIFFUSE-PLUS-FOCAL FDG UPTAKE

- Diffuse component is most often attributable to benign entities, especially chronic lymphocytic thyroiditis.
- The underlying pathology of the focal component would appear to be more heterogeneous, including benign Hashimoto's thyroiditis, adenomatous goiter and thyroid malignancy.
- Patients with the diffuse-plus-focal uptake should be investigated in a manner similar to patients with focal uptake.

SELF-RESOLVING VARIANT

- In study of 6457 FDG-PET scans, we identified 103 patients with incidental focal thyroid uptake (PETomas), and unexpectedly 5 patients (4.9%) demonstrated self-resolution of the PETomas.

- The reasons underlying this process are unknown

TUMOR TYPES AND UPTAKE PATTERNS

- Papillary thyroid cancer accounts for nearly 90% of all cases of thyroid carcinomas.
- Primary thyroid carcinomas would be expected to make up the majority of thyroid incidentalomas, however it is important to recognize that metastases and thyroid lymphomas have also been described.
- This is significant as it may prompt a change in prognosis and treatment
- A meta-analysis identified 1.1% of PET-detected thyroid incidentalomas to represent metastatic disease.

Table 2. Types of malignancies diagnosed in PET-detected thyroid incidentalomas by pattern of uptake

Authors	#PET/CT scans	FDG uptake pattern	Differentiated	Medullary	Anaplastic	Lymphoma	Metastasis
Ceriani *et al.*[25]	12,652	Focal	24	1	1	1	3 (sarcoma, renal, esophageal)
Beck *et al.*[40]	35,124	Focal	48	0	0	2	9
Gedberg *et al.*[26]	2451	Focal	9	1	0	0	0
Ozderya *et al.*[42]	6873	Focal	23	1	0	0	3 (lung 2, esophagus)
Makis *et al.*[43]	7252	Focal	12	0	0	1	1 (renal)
Kim *et al.*[24]	18,172	Focal	51	0	0	0	0
Chun *et al.*[29]	2584	Focal	14	0	0	0	1 (SCC esophagus)
Brindle *et al.*[33]	7221	Focal	6	0	0	1	0
Lee *et al.*[30]	2368	Focal	8	0	1	0	2 (melanoma, adenocarcinoma)
Nishimori *et al.*[18]	6457	Focal	9	0	0	0	0
Chen *et al.*[45]	2594	Focal	5	0	0	0	2 (H&N SCC, NHL)
Ishimori *et al.*[8]	1912	Diffuse	6	0	0	0	0
Kurata *et al.*[46]	1626	Diffuse Diffuse + focal	1 2	0 0	0 0	0 0	0 0
Choi *et al.*[16]	1763	Focal	16	0	0	1	1 (esophageal SCC)
Cumulative	101,797		234	3	2	6	22

#Number of PET/CT scans.

IMAGING CHARACTERISTICS

- Focal thyroid incidentalomas are reported at higher frequencies than diffuse lesions, and the associated rate of malignancy is greater.

IMAGING CHARACTERISTICS

Imaging characteristics, such as the magnitude of FDG uptake, have been postulated to adjust for malignancy risk.

STANDARDIZED UPTAKE VALUE

- Standardized uptake values (SUV) : to quantify the magnitude of FDG uptake on PET/CT.

- Several studies have evaluated the ability of SUV max to discriminate malignant from benign thyroid incidentalomas with conflicting conclusions.

SUV

Normalizes the amount of FDG accumulation in a ROI to the:

- Total injected dose
- Patients body weight

$$SUV = \frac{Mean\ selected\ \ region\ activity\ (mCi/ml)}{injected\ dose\ (mCi)/body\ weight\ (kg)}$$

Table 3. SUV_{max} values in benign versus malignant PET-detected thyroid incidentalomas

Authors	Benign SUV_{max}	Malignant SUV_{max}	*P* value
Ceriani *et al.*[25]	6.71	10.81	0.0146[a]
Ozderya *et al.*[42]	6.1	11.3	0.01[a]
Sencan Eren *et al.*[35]	4.6	8.8	< 0.05
Chun *et al.*[29]	2.8	4.7	0.001
Brindle *et al.*[33]	5.4	9.9	< 0.05[a]
Lee *et al.*[30]	3.62	5.47	0.126
Nishimori *et al.*[18]	5.2	5.8	0.36
Kang *et al.*[44]	3.56	6.32	< 0.05
Chen *et al.*[45]	2.9	4.0	> 0.05
Choi *et al.*[16]	6.7	10.7	< 0.05

SUV

- Mitchell *et al*. reported that using a SUVmax cutoff value of 5.0 resulted in 60% sensitivity and 91% specificity for detection of malignancy, while Boeckmann *et al* proposed a cutoff value of 4.2.
- Some reports noted a significant difference in SUVmax between malignant and benign lesions while others showed no difference at all.
- Recall that benign and malignant oncocytic/Hürthle cell lesions are known to exhibit high FDG-avidity due to an intrinsic mitochondrial defect resulting in inefficient glucose metabolism.

SUV

- Small tumors, including many thyroid incidentalomas, may not be accurately quantified on PET imaging due to the partial-volume effect.

- It is generally thought that the limit of resolution for PET/CT uptake is 5-8 mm, although the partial volume effect may impact SUV values in lesions measuring 2 to 3 times the spatial resolution.

ALTERNATIVE RADIOTRACER IMAGING

^{18}FDG-PET/CT imaging accounts for most PET-identified thyroid incidentalomas, but this is increasingly recognized on other forms of functional imaging such as ^{68}Ga-DOTATATE, ^{68}Ga PSMA, and 18F- or 11C-choline PET/CT scans.

^{68}GA-DOTA PET/CT

- Evaluate and monitor neuroendocrine tumors expressing somatostatin receptors with a sensitivity and specificity as high as 96% and 100%, respectively.

- 68Ga- and 64Cu-DOTATATE are currently the only peptides clinically approved by the FDA in the USA for PET imaging. (Ga=68 min, Cu=12 hours)

- Physiologic uptake has been noted in the pituitary, thyroid, spleen, liver, adrenal glands, head of the pancreas, and urinary tract

^{68}GA-DOTA PET/CT

- Normal thyroid tissue expressed somatostatin transmembrane receptors (SSTR), typically resulting in very low, diffuse uptake

- High *SSTR2* expression has been noted in differentiated thyroid cancers and benign thyroid conditions, but it is unclear if this uptake pattern varies from baseline physiologic uptake.

- Activated lymphocytes are known to express SSTR. Thus benign inflammatory conditions such as thyroiditis, trauma, or surgery may induce abnormal uptake.

^{68}GA-DOTA PET/CT

- Importantly, medullary thyroid cancers would be expected to be highlighted on 68Ga-DOTATATE PET/CTs.

- However low or variable *SSTR* expression may give false-negative results.

- These scans are also subject to spatial resolution limitations.

^{68}GA-DOTA PET/CT

Studies have shown a 4.1%- 11% rate of detection of thyroid incidentalomas on Ga-Dotatae , with an average of 2.6% showing diffuse uptake (thyroiditis?).

^{68}GA-DOTA PET/CT

- Nockel *et al* evaluated 237 ^{68}Ga-DOTATATE scans to assess the uptake patterns in the thyroid gland.
- Abnormal thyroid uptake was noted in 11% (26 of 237), with 14 displaying focal uptake and 12 with a diffuse pattern.
- Three of the focal lesions were found to be differentiated thyroid cancers (21.4% of focal incidentalomas).
- No significant difference was noted in SUVmax values between benign and malignant

^{68}GA-DOTA PET/CT

- Kohlenberg *et al* thyroid lesions with focal 68Ga-DOTATATE PET/CT uptake, in 4.9% of scans (94 of 1927).
- Notably, four patients were imaged for the staging of a known medullary thyroid cancer.
- Five patients (one multifocal) were diagnosed with medullary thyroid cancer, one of which was discovered incidentally due to this imaging.
- As expected, the baseline calcitonin levels were quite elevated in MTC patients.

It certainly seems reasonable to consider calcitonin assessment in patients with 68Ga-DOTATATE avidity.

^{68}GA-PSMA

- Stage and monitor prostate cancer by binding prostate-specific membrane antigen (PSMA)
- PSMA is expressed in normal prostate epithelium and highly expressed in prostate carcinoma.
- several other solid tumor types, including thyroid carcinomas (classical PTC, follicular thyroid carcinoma, and iodine-refractory cancers).
- All evaluated metastatic lesions exhibited *PSMA* expression compared to only 67% of lymph node metastases.
- In a study of 10 patients with metastatic differentiated thyroid cancer, 68Ga-PSMA PET/CT identified 30 of 32 metastatic lesions.
- These findings may advocate for use of this imaging for evaluation of suspected metastatic disease, particularly in radioiodine-refractory tumors

^{68}GA-PSMA

- Incidental 68Ga-PSMA thyroidal uptake is rare, the literature being punctuated mostly by single case reports.
- In a systematic review published in June 2019, Bertagna *et al* collected a total of 23 cases of PSMA thyroid incidentaloma from 12 papers.
- Among these 23 patients, malignancy was documented in 6.
- 5 primary thyroid (4 papillary thyroid carcinoma, one follicular thyroid carcinoma)
- one metastasis from renal cell carcinoma.

^{68}GA-PSMA

- Gossili *et al* reported on their study of 341 patients with prostate cancer who had undergone 68Ga-PSMA PET/CT scanning, identifying 13 patients (4%) with incidental increased thyroid uptake.

- The pattern of uptake was focal in seven, diffuse in five and diffuse-plus-focal in one.

- Malignancy was confirmed in 2 patients (2/13, 15%), and both displayed focal uptake.

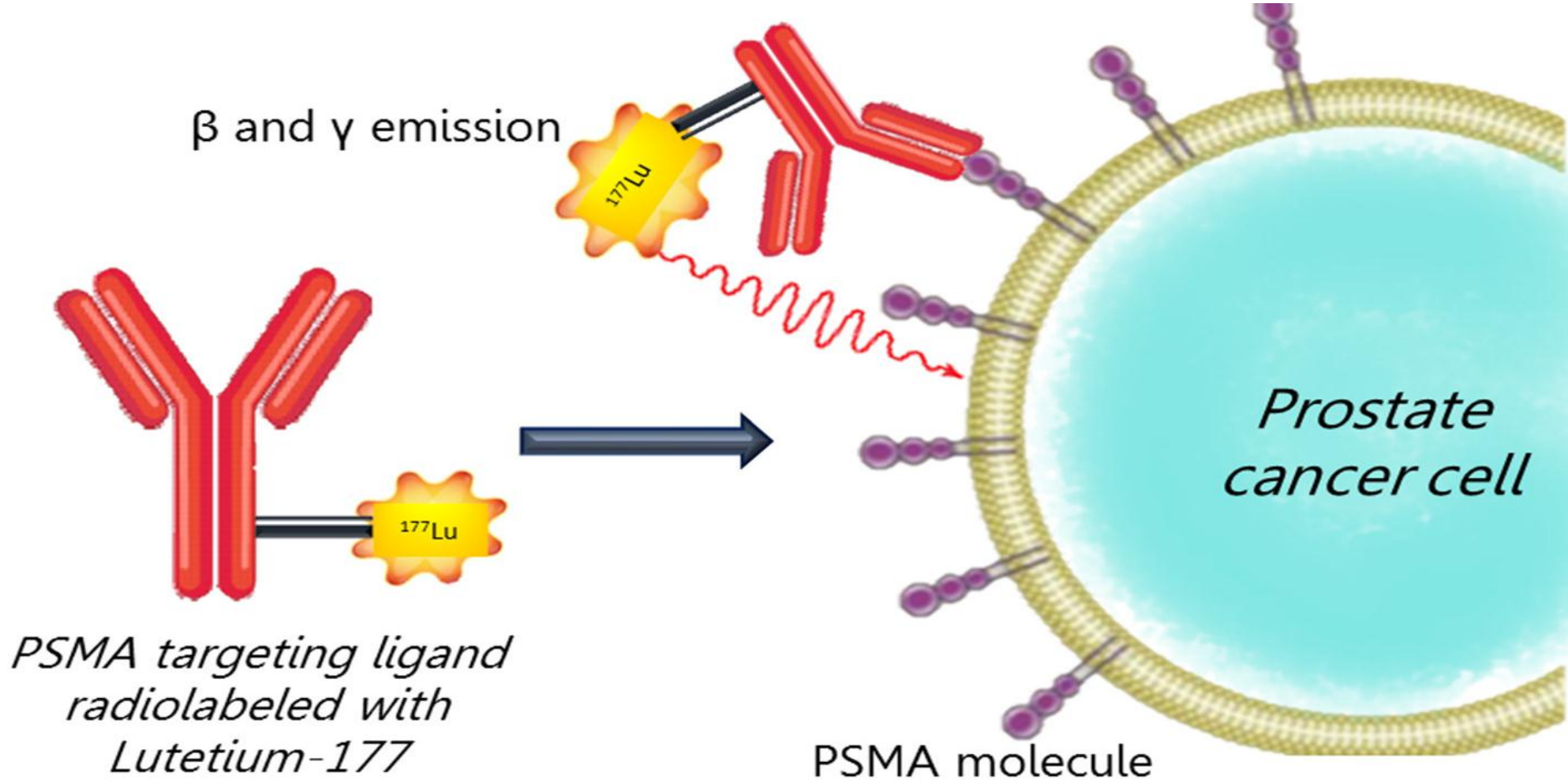
^{68}GA-PSMA

- Further investigations in patients found to have focal thyroidal uptake on PSMA-based PET imaging, namely thyroid ultrasound and biopsy.
- It is very likely that the true prevalence of PSMA-PETomas is higher since the present application of this imaging modality is for prostate cancer, thereby excluding female patients who are known to have an incidence of thyroid disorders.

^{68}GA-PSMA

Potential benefits of detecting neovasculature in advanced metastatic radioiodine refractory thyroid cancer.

TREATMENT WITH LU-PSMA????



The targeting ligand binds to PSMA on prostate cancer cells. Once bound to the neoplastic cell, 177Lu atom releases energetic β and γ particles. This results in a DNA-damaging radiation.

RADIOLABELED CHOLINE (18F OR 11C)

- Imaging several solid tumors, including potential for imaging parathyroid adenomas and hyperplasia.
- Choline is a precursor to the phosphatidylcholine that comprises much of the cellular membrane.
- Increased uptake is noted in conditions with high proliferative rates.

RADIOLABELED CHOLINE (18F OR 11C)

- In a retrospective analysis by Ruiz-Esponda *et al* 30 thyroid incidentalomas were identified in a pool of 1197 radiolabeled choline PET/CT scans (2.5%).

- Of the 15 patients that underwent diagnostic FNAC only one malignancy was identified, indicating that incidental thyroid lesions detected by this method may have a lower likelihood of malignancy than those detected by FDG-PET/CT.

MUTATION ANALYSIS

- In recent years across various cancers as a method to improve the characterization of tumors and associated prognosis.

- *BRAFV600E* is the commonest mutation encountered in adults with thyroid cancer, occurring in close to 50% of patients with papillary thyroid carcinoma.

- Studies have shown that a *BRAF* mutation in papillary thyroid cancer is associated with worse outcomes, commonly reported as a higher stage at diagnosis and more frequent distant metastases. (??????????)

MUTATION ANALYSIS

- Higher risk of death has also been described with *BRAF*-mutated thyroid cancers, on the order of 2.66-fold higher.

- It has been reported that male gender is a robust independent risk factor for PTC-specific mortality in BRAFV600E patients but not in wild-type BRAF patients .

MUTATION ANALYSIS

- In a study comparing PET-detected papillary thyroid cancers to conventionally detected controls, Beck *et al*. described a higher rate of *BRAF* mutations in the PET-detected cohort (78% *vs*. 41%).

- In this report, the PET-detected cancers were more commonly found in males and higher stages.

MUTATION ANALYSIS

BRAFV600E mutation is associated with increased expression of glucose transporters (GLUT-1) in papillary thyroid cancers, which may be responsible for the higher proportion of *BRAF* mutations in PET-detected cancers.

MUTATION ANALYSIS

- Several studies have shown significantly higher SUVmax values in *BRAF*-mutated papillary thyroid cancers versus their BRAF-wild type counterparts.
- *GLUT* transporter expression was also noted to be elevated in thyroid incidentalomas exhibiting loss of the onco-suppressor gene *PTEN.*

- lack of *PTEN* expression in thyroid cancer cells was responsible for GLUT-1 upregulation and glucose uptake.

- Aggressive, poorly differentiated thyroid cancers have higher levels of *GLUT-1* expression.

MUTATION ANALYSIS

Increased expression of *GLUT* transporters in both *BRAF* and *PTEN* mutated phenotypes ➡ PET-detected thyroid incidentalomas exhibiting more aggressive behavior.

MUTATIONS IN THE *P53*

- Mutations in the *p53* tumor suppressor gene are exhibited in nearly 50% of all cancers yet are identified in only 10% of thyroid cancers.
- In a retrospective study of patients with PET-detected thyroid cancers, 86% of those that underwent operation were found to express *p53* mutations (significance?).

MANAGEMENT RECOMMENDATIONS

- Clinical guidelines for the management of thyroid nodules in the general population are well Established.

- Most PET/CT imaging is pursued to evaluate another malignancy that may limit life expectancy, it is difficult to determine if these guidelines should apply to this population.

- Different in prognosis, economy, comorbidities and …

MANAGEMENT RECOMMENDATIONS

- Thyroid cancer is associated with an excellent prognosis, with overall 10-year survival rates of differentiated thyroid cancers exceeding 90%-95%.
- For example, in patients that underwent cytologic diagnosis of an incidental thyroid cancer, the risk of death from thyroid cancer was < 1%.

MANAGEMENT RECOMMENDATIONS

- Studies of active surveillance of low-risk papillary microcarcinomas (cytologically confirmed PTC with nodule diameter ≤ 1 cm without high-risk features) have shown safety with this approach.

- Only 7%-8% of observed nodules increased in size, and there were no instances of recurrence or death following salvage surgery.

MANAGEMENT RECOMMENDATIONS

Are *et al* suggested that PETomas (incidentalomas) are associated with a poorer prognosis due to a higher rate of unfavorable pathologic features such as tall cell variant, poor differentiation, and extrathyroidal extension.

MANAGEMENT RECOMMENDATIONS

- Although most thyroid carcinomas are associated with an excellent prognosis, it does seem prudent that each incidentally discovered thyroid lesion be carefully evaluated for risk factors.

- Review of prior images should be conducted to evaluate the evolution of the noted lesion over time. PET scans may reveal signs of lateral lymph node metastases. (poorer prognosis & surgical plans).

- Younger age, male gender , childhood radiation exposure , and family history of thyroid cancer.

MANAGEMENT RECOMMENDATIONS

- Current clinical guidelines recommend further investigation, including FNAC, to evaluate all PET-identified thyroid incidentalomas greater than 1 cm in diameter.
- A study utilizing SEER data in USA found that only tumor size > 2.5 cm was associated with an increased mortality.
- Another population-based study found size > 2 cm, microcalcifications, and solid composition related to increased malignancy risk.
- The risk of cancer in solid lesions has been reported at 13% compared to 4% for mixed solid/cystic lesions

SEER: Cancer database in USA

MANAGEMENT RECOMMENDATIONS

- Ultrasound has been the mainstay of imaging thyroid nodules.
- Several risk stratification systems (ACR-,EU-, and K-TIRADS) have been developed, however, it is open for debate if these systems are applicable to PET-detected thyroid incidentalomas.
- Previous investigators have proposed that these lesions have a greater likelihood of high-risk features which may make these stratifications schemes unreliable.

MANAGEMENT RECOMMENDATIONS

- Trimboli *et al* examined the ability of EU-TIRADS to appropriately stratify focal PET-detected thyroid incidentalomas.
- Of the 13 confirmed malignancies included in this study, 11 were categorized as EU-TIRADS 5, 1 as EU-TIRADS 4, and 1 as EU-TIRADS 3.
- SUVmax also found to be significantly higher in the cancer population, with the most accurate cut-off values determined as > 7.1.

MANAGEMENT RECOMMENDATIONS

- The presence of one of these risk factors (SUVmax > 7.1, or EU-TIRADS 5) detected 12 of 13 cancers (92% sensitivity) .
- Absence of these features detected 34 or 35 benign lesions (97% specificity).

- Given the higher likelihood of cancer in this population, EU-TIRADS and KTIRADS were advocated as the preferred stratification tools due to the greater number of FNAC recommended.

MANAGEMENT RECOMMENDATIONS

- An otherwise healthy patient should receive the full measure of workup and treatment as indicated by current guidelines.
- In patients with life-limiting malignancies or comorbidities should be approached with further evaluation.
- Thoughtful consideration of patient factors (age, comorbidities, quality of life), underlying malignancy (prognosis, required treatment), and local radiologic features are mandatory.

MANAGEMENT RECOMMENDATIONS

- The risk of intervention must be weighed against the potential benefits.
- Further evaluation with dedicated ultrasound imaging incites little risk, and FNAC should be considered if appropriate per TIRADS recommendations.
- Confirmation of metastasis or thyroid lymphoma would be expected to drive a change in treatment approach.
- Diagnosis of a papillary thyroid cancer may prompt consideration of active surveillance due to the generally indolent nature of this condition, or surgical management if the patient's condition permits.

SUMMARY OF RECOMMENDATIONS

1. Assess the patient's clinical condition, considering the index cancer, comorbidities, and frailty.

If unacceptable for further intervention, reassess for possible intervention as status changes.

2. For those with focal PET/CT thyroid avidity that is amenable to further intervention, neck ultrasound should be obtained, with FNAC pursued based on TIRADS guidelines.

3. In thyroid incidentalomas discovered on ^{68}Ga-DOTATATE PET/CT, consider obtaining a baseline

calcitonin level.

SUMMARY OF RECOMMENDATIONS

4.No imaging features or patterns of uptake can definitively discern benign from malignant lesions (SUV???).

5. Active surveillance of a well-differentiated thyroid carcinoma can be considered during active

management of the baseline malignancy; however, it should be acknowledged that some

PET-detected thyroid incidentalomas may represent more aggressive malignancies.

CONCLUSION

Clinicians must employ the art of medicine and carefully balance the risks and benefits of pursuing further workup and management while taking into account the underlying condition and expectations of the patient.


Thanks For Attention