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HEAD AND NECK

# Unfolding the role of PET FDG scan in the management of thyroid incidentaloma in cancer patients

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**Abstract** Thyroid incidentaloma detected on FDG-PET scan has been reported repeatedly in the last several years, though conflicting data are reported. Our aim is to identify the incidence and outcome of incidental FDG-PET detected thyroid lesions in patients undergoing FDG-PET scan for other primary malignancies and to suggest a management algorithm. This is a retrospective review of all patients who had a FDG-PET detected incidental thyroid lesion between January 2002 and December 2009 at Peter MacCallum Cancer Center. Demographics, data relating to PET scan findings, FNA diagnoses, operative details, and histopathology were reviewed. Of the 1,034 subjects who underwent the FDG-PET study, 51 (4.9 %) were identified as having thyroid incidentaloma, 31 females and 20 males with a mean age of 60 years. Thyroid malignancy was noted in 39.5 % (19/48 patients) who underwent FNAB. Sixteen underwent thyroidectomy. The histopathology revealed 12 patients with papillary carcinoma, 5 with follicular carcinoma and 2 with medullary carcinoma. The high rates are in concordance with analysis of the rates published in the literature. In patients with thyroid PET incidentaloma, the incidence of primary thyroid malignancy is very high as reported in our study and based on analysis of published data, necessitating further investigation. If assessment of these incidentalomas suggests malignancy, then appropriate surgical management may be warranted according to the patient's medical condition.

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## Introduction

Thyroid cancer rates have increased worldwide in the last decades, and this dramatic increase has been attributed to the detection of subclinical disease, as there is no corresponding increase in disease-specific mortality rates [1]. This increase is probably related to the fact that thyroid incidentalomas which are defined as newly identified thyroid lesions encountered during imaging studies are more frequently detected lately [2].

Positron emission tomography (PET) with fluoro deoxy glucose (FDG) is a whole-body imaging technique that detects the increased rate of glycolysis in tumor cells [3]. PET scanning is increasingly being undertaken for a variety of malignancies and is becoming the imaging modality of choice for staging. Incidental FDG-PET abnormalities unrelated to the primary tumor occur in at least 5 % of scans, and in most cases the clinical scenario will dictate the extent to which these incidental findings need to be investigated.

Thyroid incidentaloma detected on FDG-PET scan has been reported repeatedly in the last several years. Cohen et al. [4] reported in a retrospective review of FDG-PET studies that thyroid incidentaloma was found in 2.3 % of a group of patients who underwent FDG-PET for the metastatic evaluation of cancer, and 47 % of those incidentalomas, with an available pathological diagnosis, turned out to be malignant. Several other retrospective studies have reported that PET thyroid incidentalomas were found in 0.02–8.4 % of cancer patients or healthy subjects on PET examinations [4–19]. The risk of malignancy ranged from 13 to 59 % in those studies (Table 1). The incidence of

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**Table 1** Data presented in recent studies by rates of further workup

| Series | Population | Number of patients | PET incidentalomas (%) | Incidentalomas that underwent FNA or surgery (%) | Thyroid malignancies (%) |
|---|---|---|---|---|---|
| Cohen et al. [4] | Cancer | 4,525 | 102 (2.3) | 15 (15) | 7 (47) |
| Are et al. [5] | Cancer | 11,500 | 377 (3.2) | 61 (16) | 24 (39) |
| Bae et al. [6] | Cancer | 3,379 | 285 (8.4) | 99 (35) | 22 (23) |
| Ishimori et al. [7] | Cancer | 1,912 | 29 (1.5) | 11 (38) | 6 (24) |
| Kang et al. [8] | Healthy and cancer | 1,330 | 29 (2.2) | 15 (52) | 4 (27) |
| Bogsrud et al. [9] | Cancer | 7,347 | 79 (1.1) | 48 (61) | 15 (35) |
| Nam et al. [10] | H&N cancer | 689 | 19 (2.7) | 12 (63) | 5 (41) |
| Choi et al. [11] | Healthy and cancer | 1,763 | 70 (3.9) | 45 (64) | 17 (37) |
| Even-Sapir et al. [12] | Cancer | 2,360 | 59 (2.5) | 41 (69) | 13 (31.7) |
| Kim et al. [13] | Cancer | 4,136 | 45 (1) | 32 (71) | 16 (50) |
| Nilsson et al. [14] | Cancer | 3,641 | 37 (1) | 27 (73) | 16 (59) |
| Zhai et al. [15] | Cancer | 3,580 | 115 (3.2) | 96 (83) | 48 (50) |
| Chen et al. [16] | Healthy | 4,803 | 60 (1.2) | 50 (83) | 7 (14) |
| Kim et al. [17] | Cancer | 11,623 | 159 (1.3) | 140 (88) | 37 (26) |
| King et al. [18] | Cancer | 15,711 | 22 (0.1) | 22 (100) | 3 (13) |
| Kurata et al. [19] | Healthy | 1,626 | 4 (0.02) | 4 (100) | 2 (50) |
| Our study | Cancer | 1,025 | 51 (4.9) | 48 (94) | 19 (39.5) |

thyroid FDG-PET incidentaloma is increasing as PET Scans are utilized more frequently, creating management queries as malignancy is being detected in various rates.

Our objective is to identify the incidence and outcome of incidental FDG-PET detected thyroid lesions in patients undergoing FDG-PET scan for other primary malignancies in our cancer dedicated institution, to review the literature and calculate the prevalence of malignant incidental thyroid lesions identified by FDG-PET, and to suggest a practical algorithm for their management.

## Materials and methods

The study was approved by Peter MacCallum Cancer Center Surgical Oncology Department Review Board. A retrospective review of all patients who had a FDG-PET detected incidental thyroid lesion between January 2002 and December 2009 was performed. The patients who were eligible for this study were being scanned on the basis of a diagnosis of non-thyroidal malignancy and had an unequivocal incidental thyroid uptake. Included were patients who had undergone further workup regarding the thyroid incidentaloma. Patients with a known thyroid carcinoma were excluded, as were patients with thyroid metastatic disease from the known primary malignancy. Cases in which the thyroid lesion was known prior to performing the PET scan, or those who had FNA of a thyroid lesion prior to performing the PET scan were excluded.

The PET scan was performed with PET CT system (Discovery LS, GE Medical Systems, Waukesha, WI, USA). Examinees were required to fast for at least 8 h before the PET scan and avoid strenuous work or exercise for 24 h before the scan. PET/CT imaging was performed 60 min after injection of F-18 FDG. Emission images were acquired for 5 min per bed position. The uptake period between FDG injection and the beginning of the emission scan was 60 min.

Thyroid incidentaloma was defined as thyroid uptake identified on FDG-PET study incidentally, and it was divided into focal and diffuse types according to the thyroid uptake pattern of FDG. Focal uptake was defined as FDG uptake in less than one lobe and was further evaluated.

FNA was performed with a 21-gauge needle on a 10-ml syringe under ultrasonographic guidance. Two passes were made per nodule and specimens were smeared on slides. The procedure was performed by an experienced radiologist and the cytological diagnosis was made by an experienced pathologist.

### Statistics

Statistical analysis was carried out for the patient group by computing the mean and standard deviation. Statistical differences were analyzed using one-way analysis of variance (ANOVA) followed by Student's *t* test. The level of statistical significance was set at $p < 0.05$.

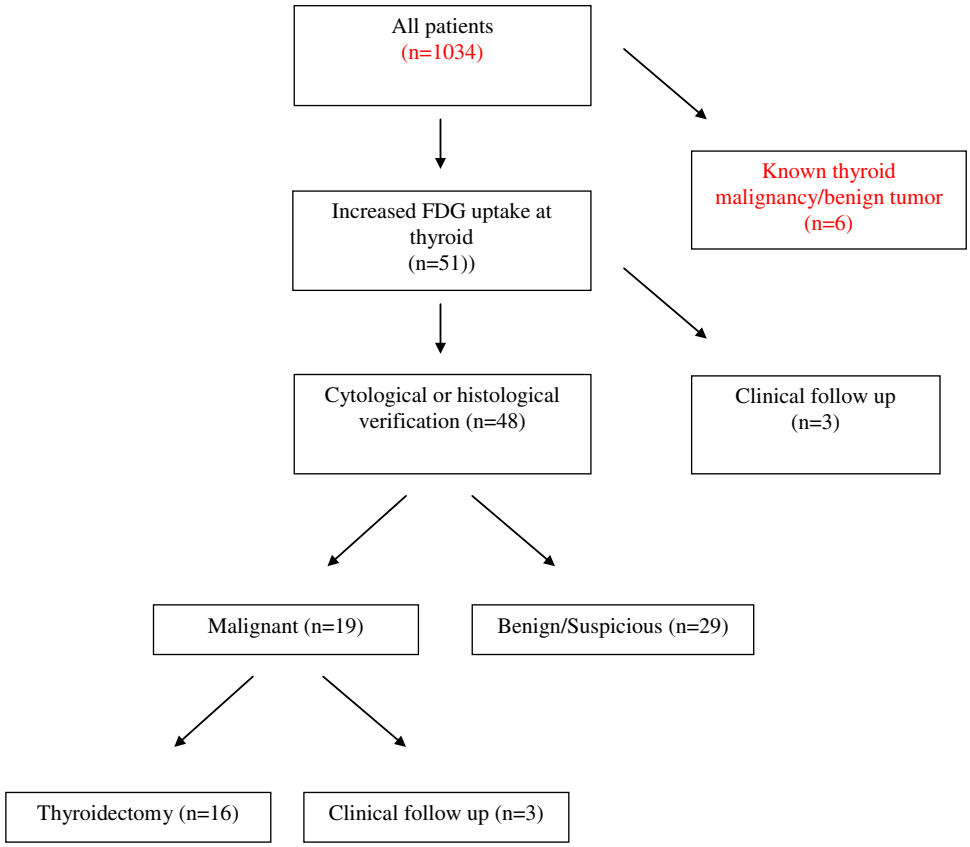


**Fig. 1** Flow of the participants ($n = 1{,}034$) through the study

## Results

Of the 1,034 subjects who underwent the FDG-PET study, 51 (4.9 %) were identified as having thyroid incidentaloma, 31 females and 20 males with a mean age of 60 years (25–81). Thirty-eight patients have had the PET scan for index malignancy diagnosis, 648 for restaging of the index malignancy and 342 for staging and radiotherapy planning. Three patients have had PET scan for evaluation of papillary thyroid cancer metastasis and therefore they were not included. Two patients have had undergone total thyroidectomy and were evaluated for suspected recurrence and were also not included as was one who was known to have a pathologically proven benign thyroid nodule. Three patients had had a previous diagnosis of benign thyroid disease but none had undergone FNAB or surgery and were therefore included in our study. In 3 others, the focal thyroid uptakes were not addressed due to their clinical condition and no diagnostic workup was done, therefore these patients were excluded from our study (Fig. 1).

Intra-abdominal malignancy in 15 patients was the commonest indication for PET scan along with 6 patients with melanoma, 5 patients with lung malignancy, 9 patients with head and neck tumor, 8 patients with hematological malignancies, 4 patients with soft tissue tumor and 1 patient with renal tumor (Table 2).

**Table 2** Indication for PET scan

| Primary malignancy | No. |
|---|---|
| GI, Gynecology | 15 |
| H&N | 9 |
| Hematological | 8 |
| Melanoma | 6 |
| Lung | 5 |
| Soft tissue sarcoma | 4 |

Prior to the PET scan, 13 patients had undergone chemotherapy and 16 had radiotherapy, of which were 7 patients who underwent both treatments. Four patients who had received radiotherapy previously to the head and neck, were found to have follicular carcinomas in three cases.

Neoplastic thyroid lesions were diagnosed in 19 of 48 patients (39.5 %): papillary thyroid cancer in 12, follicular carcinoma in 5, medullary carcinoma in 2 patients and metastatic lesions (malignant melanoma and cutaneous squamous cell carcinoma) in 2 patients. The median size of the excised primary lesions was 15 mm (6–55 mm). Surgical treatment was not offered in the 2 cases found to have medullary carcinoma and in 1 case with papillary carcinoma due to the patient's medical condition (Fig. 1).

**Table 3** Data grouping from published studies showing absolute rates of malignancy in group A and B

| | PET incidentalomas (%) | Thyroid malignancies (%) | |
|---|---|---|---|
| Group A: series with low rates of further workup (<55 %) | | | |
| Cohen et al. [4] | 102 (2.3) | 7 (47) | |
| Are et al. [5] | 377 (3.2) | 24 (39) | |
| Bae et al. [6] | 285 (8.4) | 22 (23) | |
| Ishimori et al. [7] | 29 (1.5) | 6 (24) | |
| Kang et al. [8] | 29 (2.2) | 4 (27) | |
| Sum | 822 | 63 | 7.6 % |
| Group B: series with high rates of further workup | | | |
| Bogsrud et al. [9] | 79 (1.1) | 15 (35) | |
| Nam et al. [10] | 19 (2.7) | 5 (41) | |
| Choi et al. [11] | 70 (3.9) | 17(37) | |
| Even-Sapir et al. [12] | 59 (2.5) | 13 (31.7) | |
| Kim et al. [13] | 45 (1) | 16 (50) | |
| Nilsson et al. [14] | 37 (1) | 16 (59) | |
| Zhai et al. [15] | 115 (3.2) | 48 (50) | |
| Chen et al. [16] | 60 (1.2) | 7 (14) | |
| Kim et al. [17] | 159 (1.3) | 37 (26) | |
| King et al. [18] | 22 (0.1) | 3 (13) | |
| Kurata et al. [19] | 4 (0.02) | 2 (50) | |
| Sum | 669 | 179 | 26.7 % |

## Discussion

Incidental thyroid lesions are increasingly detected with the routine use of radiological investigations such as US, CT scan and MR imaging [20], with certain features suggestive of malignancy e.g., microcalcification on US [21]. However, due to its relatively recent introduction, there are still no definitive PET criteria to help diagnose malignancy in thyroid incidentalomas. The high rates of PET detected thyroid incidentalomas (0.02–8.4 %) highlight the importance of excluding thyroid cancer. Some have reported on factors that increase the likelihood of thyroid cancer when evaluating PET detected thyroid incidentalomas. The presence of physical finding and the average SUV were regarded as factors that significantly correlate with an increased risk of malignancy, although controversy still exists in the literature [5, 17].

Thyroid PET incidentaloma has been found to be malignant in 14–59 % of cases [4–19]. In the current study, the prevalence of malignancy of thyroid PET detected incidentalomas was 39.5 % (Table 1). The high prevalence of malignant disease reported by some suggests that focal thyroid PET incidentaloma should have further diagnostic workup such as FNAB and the possibility of further surgical management. However, there is a potential for patient bias as there was wide variation in the extent of diagnostic workup, ranging from 15 to 100 % (Table 1). In addition, due to the retrospective nature of all the studies, the management of the thyroid incidentalomas may be influenced by the patients' index cancer.

In our cohort, we report of a very high rate of additional workup (94 %) for PET thyroid incidentalomas, and a high rate of malignancy (39.5 %). In trying to summarize the reported data in the last several years, we compared studies reporting lower rates of thyroid PET incidentalomas workup (<55 %) (group A) with those reporting higher rates of thyroid PET incidentalomas workup (group B) (Table 3). The difference between the groups is significant. Although half of the studies in group A reported a 40–50 % of malignancies in their PET thyroid incidentalomas, due to the low rate of additional workup, only 7.6 % of their total cohorts were histologically proven to be malignant. In group B, the rate of reported malignant findings was not different from group A but in contrast to group A, the rate of histologically malignancy in the entire cohort in group B tripled, reaching 26.7 %.

The possible cause for a low rate of workup in these patients is probably related to their medical condition. We assume that some of them have not gone through proper management of their thyroid incidentalomas due to their seemingly unimportance in the patients' eyes. One can even argue for the possibility that the treating physician's focus should be on the more aggressive cancer being treated moving aside the lower grade thyroid cancer.

However, most of the cancer patients are in the age in which worse prognosis is encountered in differentiated thyroid cancer. Since the proper management of incidental

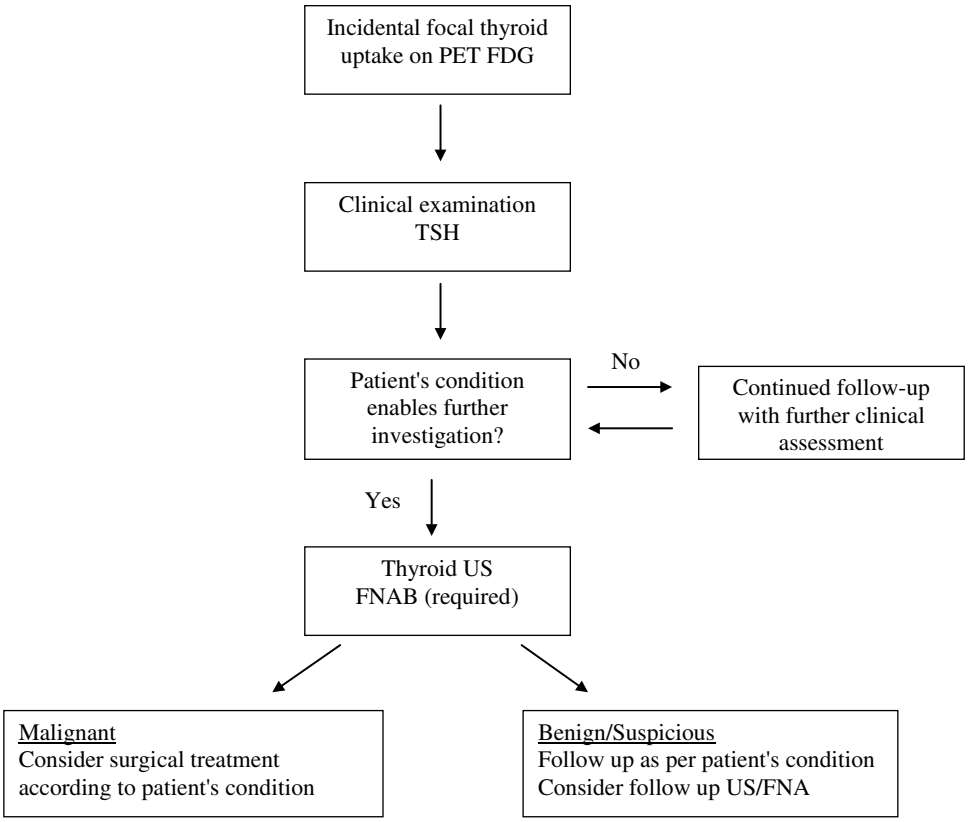


**Fig. 2** Practical algorithm for management for focal thyroid uptake in cancer patients

thyroid lesion is cost worthy and simple to utilize, we would strongly suggest further workup in those cases as is illustrated in Fig. 2. This flow chart is easy to work by even in patients with high-stage malignancy, and usually requires blood test, neck US and FNAB. These can easily be done in most cases of patients treated for other types of malignant tumors as is demonstrated in our cohort. Furthermore, if differentiated thyroid cancer is proven histologically, it will be a low staged disease as it was an asymptomatic mass, and the management will usually include hemi or total thyroidectomy, which is considered common surgery with a low rate of complications. On the other hand, a neglected differentiated thyroid cancer will grow and metastasize, necessitating wider surgical resection and post-operative treatment, which might be challenging in a setting of management of another violent malignant disease.

Taking all the above into consideration, a low rate of further workup in these patients is not adequate. We would recommend further expert workup which needs to include physical examination and obtaining TSH levels in all cases to exclude hyper or hypothyroidism and extensive neck disease. In most cases in which further workup is feasible, we recommend performing an US-guided FNA. In malignancy proven cases, further surgery may be warranted, depending on the patient's medical condition.

## Conclusion

In patients with thyroid PET incidentaloma, the incidence of primary thyroid malignancy is very high as reported in our study and based on analysis of all published data, necessitating further investigation. If assessment of these incidentalomas suggests malignancy, then appropriate surgical management may be warranted according to the patient's medical condition.

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