

1-6-2011

# Focal thyroid incidentalomas identified with whole-body FDG-PET warrant further investigation.

Ruth S. Prichard

*Royal College of Surgeons in Ireland*

M Cotter

*St. Vincent's University Hospital, Dublin*

D Evoy

*St. Vincent's University Hospital, Dublin*

D Gibbons

*St. Vincent's University Hospital, Dublin*

C Collins

*St. Vincent's University Hospital, Dublin*

*See next page for additional authors*

---

## Citation

Prichard RS, Cotter M, Evoy D, Gibbons D, Collins C, McDermot E, Skehan S. Focal thyroid incidentalomas identified with whole-body FDG-PET warrant further investigation. *Irish Medical Journal*. 2011;104(6):177-9.

This Article is brought to you for free and open access by the Department of Surgery at e-publications@RCSI. It has been accepted for inclusion in Surgery Articles by an authorized administrator of e-publications@RCSI. For more information, please contact [epubs@rcsi.ie](mailto:epubs@rcsi.ie).

---

**Authors**

Ruth S. Prichard, M Cotter, D Evoy, D Gibbons, C Collins, E McDermott, and S Skehan

**Attribution-Non-Commercial-ShareAlike 1.0**

**You are free:**

- to copy, distribute, display, and perform the work.
- to make derivative works.

**Under the following conditions:**

- Attribution — You must give the original author credit.
- Non-Commercial — You may not use this work for commercial purposes.
- Share Alike — If you alter, transform, or build upon this work, you may distribute the resulting work only under a licence identical to this one.

For any reuse or distribution, you must make clear to others the licence terms of this work. Any of these conditions can be waived if you get permission from the author.

Your fair use and other rights are in no way affected by the above.

---

This work is licenced under the Creative Commons Attribution-Non-Commercial-ShareAlike License. To view a copy of this licence, visit:

**URL (human-readable summary):**

- <http://creativecommons.org/licenses/by-nc-sa/1.0/>

**URL (legal code):**

- <http://creativecommons.org/worldwide/uk/translated-license>
-

# Focal Thyroid Incidentalomas Identified with Whole-Body FDG-PET Warrant Further Investigation

RS Prichard, M Cotter, D Evoy, D Gibbons, C Collins, E McDermott, S Skehan  
St Vincent's University Hospital, Elm Park, Dublin 4

## Abstract

Fluorodeoxyglucose (FDG) whole body positron emission computed tomography (PET-CT) detects clinically occult malignancy. The aim of this study was to assess the prevalence and significance of focal thyroid  $^{18}\text{F}$ -fluorodeoxyglucose uptake. A retrospective review of all patients who had FDG PET-CT examinations, in a single tertiary referral centre was performed. PET scan findings and the final pathological diagnosis were collated. 2105 scans were reviewed. Focal uptake was identified in 35 (1.66%) patients. Final surgical histology was available on eight patients, which confirmed papillary carcinoma in four (20%) patients and lymphoma and metastatic disease in two patients respectively. This gave an overall malignancy rate in focal thyroid uptake of at least 33%. Thyroid incidentalomas occurred with a frequency of 2.13%, with an associated malignancy rate of at least 33% in focal thyroid uptake. The high malignancy rate associated with focal thyroid uptake mandates further investigation in medically fit patients.

## Introduction

Thyroid carcinoma remains the commonest endocrine malignancy and the National Cancer Registry in Ireland predicts a rise in its incidence, predominantly as a result of the increasing incidental detection of the disease. Thyroid incidentalomas are defined as new thyroid lesions identified on radiological grounds (ultrasound, CT, MRI, PET-CT) in patients without a prior history of thyroid disease. The relevance of these lesions remains unclear; however the clinical dilemma is how to differentiate benign from malignant thyroid disease. The incidental finding of a thyroid nodule is common. Palpable thyroid nodules have been identified in 4-7% of the population and the prevalence increases to 19-67% when high resolution ultrasonography is utilized. The majority of these lesions are benign with a malignancy rate of approximately 1.5-10%.  $^{18}\text{F}$ -FDG positron emission tomography is a combination technique of functional (PET) and anatomical (CT) images to localize sites of increased metabolic activity. As malignant and inflammatory tissues exhibit increased rates of glycolysis and glucose uptake, they demonstrate more avid tracer accumulation than normal tissues. PET-CT is being increasingly used for the staging and monitoring of patients with a wide variety of known malignancies. The aim of this study was to identify the prevalence of thyroid incidentalomas, identified with PET-CT, in a single tertiary referral centre, to identify the rate of malignant disease occurring in focal incidental thyroid uptake.

## Methods

We retrospectively reviewed 2105 patients' scans that were performed in a single institution from January 2004 to January 2009. Reports were searched electronically for the word 'thyroid' and these were reviewed to identify cases with incidental thyroid uptake. The majority of PET-CT scans were performed for diagnosis or staging of patients with known or suspected malignancy. There were no specific exclusion criteria. A total of 45 patients were identified with focal or diffuse incidental uptake in the thyroid gland. Demographic data, data related to the PET scan, and follow-up data were obtained for all patients in this study using electronic databases in the radiology and pathology departments. The clinical significance of thyroid uptake was compared to the final histological diagnosis, either on fine-needle aspiration cytology or on surgical excision specimens.

PET scans were obtained on a dedicated whole body PET-CT scanner (Discovery LS, GE, Milwaukee, USA). All patients were fasted, except for water, for 6 hours prior to their scan. A blood glucose level was taken prior to administration of FDG, and insulin was administered to reduce elevated glucose if necessary. Image acquisition occurred 60 minutes following intravenous injection of 370 MBq FDG. Standard coverage was either from skull base to upper thighs, skull vault to upper thighs for head and neck primary tumours, or whole body for patients with melanoma. Typically this required 4-7 bed positions. 3D acquisition was used, with reconstruction using OSEM. CT was performed without intravenous contrast medium, with typical acquisition parameters of 120 kVp, 80mA and 3.8mm slice thickness. Oral contrast medium was administered in a minority of cases, depending on the clinical indication for PET-CT. Data were expressed as the percentage of focal and diffuse incidental thyroid FDG uptake among the study population.

## Results

Forty-five patients (35 female and 10 male, mean age: 61.9 years) were identified with incidental thyroid uptake from the reports of the 2105 patients' scans that were retrospectively reviewed. This gave an overall prevalence of both diffuse and focal thyroid incidentalomas of 2.13%. Of the 45 cases identified, 35 patients demonstrated focal thyroid uptake giving a prevalence of 1.66%. The mean age of these patients was 64.4 years with a range of 31 to 90 years. The majority of patients were female (n=26) and most lesions were identified in the right side of the gland (n=22). Ten patients were identified with diffuse thyroid uptake, leading to a prevalence of 0.47%. The mean age of this group of patients was younger at 59.4, with a range of 51-72 years and the majority were female (n=9).

Figure 1: Management Guidelines for thyroid FDG-PET CT Incidentalomas

Of the 35 patients with focal thyroid uptake, 24 (68.6%) had a thyroid ultrasound performed. The reasons for failure to further investigate focal increased thyroid uptake was the presence of diffuse metastatic disease in six patients and poor overall medical condition in two patients. Twenty patients had a thyroid FNAC performed and of these, eight patients underwent thyroid surgery (Table 1). Of the twenty patients who had a definitive pathological diagnosis two had metastatic disease: one from a previously treated breast carcinoma and one from a known glottic squamous cell carcinoma (10%); twelve patients had benign lesions (60%); four patients had a papillary carcinoma (20%) and a further two patients had a lymphoma (10%) (Table 2). Of the ten patients who had diffuse thyroid uptake, six patients (60%) had a thyroid ultrasound which demonstrated the presence of a multi-nodular goitre. No FNAC was performed on any patient with diffuse thyroid uptake.

#### Discussion

The detection of a thyroid nodule is a common clinical finding with a prevalence of between 4% to 7% in North America<sup>1</sup>. However, what remains important is to identify which of these lesions will prove to be malignant. A thyroid incidentaloma is defined as a newly identified thyroid lesion encountered during an imaging study for non-thyroidal disease<sup>2</sup>. The use of high-resolution ultrasonography identifies these lesions in 19% to 67% of the population. The majority are benign with a malignancy rate of only 1.5% to 5%. PET scanning using <sup>18</sup>F-FDG is a non-invasive whole-body imaging technique which provides functional evidence of disease. It preferentially detects malignant lesions as a result of increased glycolysis and cellular proliferation<sup>6,7</sup>. The current prevalence of PET uptake in the thyroid (focal and diffuse) is between 0.4% to 8.9%<sup>8a-16</sup>. The incidence of incidental thyroid uptake in this study was 2.13%, which is within the range reported in literature. Increasing numbers of patients with thyroid uptake of FDG will be identified in tandem with increasing use of this imaging modality.

The reported incidence of focal thyroid FDG uptake is 1.2% to 4.3%<sup>8a-14</sup>. Of these lesions, a malignancy rate of between 14% to 57% has been reported, which is higher than with other imaging modalities<sup>9a-15</sup>. This study demonstrated an overall malignancy rate of at least 33%. There are a number of proposed reasons for the higher rate of malignancy with this form of imaging. Firstly, most PET-CT scans are performed in patients who already have a diagnosis of cancer and therefore there is a high pre-test probability of a second carcinoma being detected. Secondly, patients with focal thyroid uptake were significantly older than those with diffuse uptake which may represent the increasing incidence of papillary thyroid carcinoma with age. Thirdly, PET-CT is a functional imaging modality which identifies early malignant disease due to the increased utilization of glucose in malignant cells. Finally, most published data is retrospective, with a small cohort of patients who have final histological diagnoses which may alter the final incidence of malignant disease. However, given the high associated risk of malignancy in focal thyroid incidentalomas, further diagnostic work-up should be considered in all surgically fit patients.

In direct comparison, our rate of diffuse uptake was 0.47% which is similar to previous reports of diffuse thyroid FDG uptake of between 0.4% to 8.9%<sup>15,16</sup>. However, it is much less likely to be malignant. Studies by both Yasuda et al and Karantanis et al demonstrated that diffuse uptake is predominantly due to chronic lymphocytic thyroiditis (Hashimoto's) with a small number being due to Graves' disease<sup>15,16</sup>. While analysis of thyroid function would be advantageous this was not performed due to the retrospective nature of this study. Therefore, the management of diffuse and focal thyroid lesions should be different based on the underlying risk of malignancy (Figure 1).

The majority of thyroid carcinomas that have been identified in other studies have occurred in woman and have been papillary in nature. This study demonstrates similar results with all cancers occurring in women and all four primary thyroid carcinomas were papillary. It is important to note that the presence of a solitary thyroid nodule may be due to metastatic disease. Although the thyroid gland is an uncommon site of secondary carcinoma deposits<sup>19</sup>, this series has demonstrated that two patients, with focal thyroid uptake of <sup>18</sup>F-FDG had metastatic disease (10%)<sup>19</sup>. Therefore, while focal thyroid uptake of FDG should be considered to be more likely to represent a second primary tumour the presence of metastatic disease should also be considered. We do however accept that there may be a degree of selection bias due to the fact that the majority of PET scans were performed for patients with pre-existing malignant disease. This study used ultrasound guided final needle aspiration cytology to obtain a pre-operative histological diagnosis. This is a sensitive test with a false negative rate of 0.7% to 2.4% and an accuracy rate of 95%<sup>20</sup>.

However, it is often limited by the ability to obtain enough tissue to make a diagnosis and the difficulty in differentiating benign and malignant follicular lesions. In this series, within the focal thyroid uptake group, two patients had a thyroid lobectomy performed for a follicular and a Hurthle cell adenoma respectively. All five patients with a pre-operative T4 FNAC had malignant disease as did the one patient who had a T5 diagnosis. A limitation of this study is the difficulty in accurately predicting the sensitivity of PET-CT as eight patients with a Thy 3 follicular

lesion did not undergo surgical excision. This study has a number of limitations, primarily as a result of its retrospective nature. Firstly, in total there are only a small number of patients with either focal or diffuse uptake (n=45; 2.13%). Secondly, of the focal lesions that were identified only 57% had further imaging and a histological diagnosis obtained. This may therefore obscure the real incidence of malignancy in PET positive lesions, but it reflects a complex patient population in whom detection of a possible small thyroid neoplasm may not always be clinically relevant.

This study demonstrates that incidental focal thyroid uptake identified on PET-CT occurs in 1.66% of all scans and has as associated malignancy rate of at least 33%, significantly higher than the malignancy rate for thyroid nodules detected by any other means. Further investigation with FNA and US guided biopsy is mandatory in surgically fit patients. While it is reassuring that diffuse thyroid uptake is not considered to be related to malignancy it would however, be prudent to at least perform a thyroid ultrasound. The accurate identification of the risk of malignancy in focal thyroid lesions is important as the number of carcinomas identified in this manner is set to increase, utilizing significant resources, as the use of PET-CT becomes more widespread.

Correspondence: RS Prichard  
St Vincent's University Hospital, Elm Park, Dublin 4  
Email: [ruthprichard@rcsi.ie](mailto:ruthprichard@rcsi.ie)

#### References

1. Thyroid Carcinoma statistics. National Irish Cancer Registry 2006.
2. Tan GH, Gharib H. Thyroid Incidentalomas: management approaches to non- palpable nodules discovered incidentally on thyroid imaging. *Ann Intern Med* 1997; 126: 226 â 31
3. Burguera B, Gharib H. Thyroid Incidentalomas. Prevalence, diagnosis, significance and management. *Endocrinology and metabolism clinics of North America* 2000; 29: 187 â 203
4. Brander A, Viikinkoski P, Nickels J, Kivisaari L. Thyroid Gland: US screening in a random adult population. *Radiology* 1991; 181: 683 â 687
5. Ezzat S, Sarti DA, Cain DR, Braunstein GD. Thyroid Incidentalomas. Prevalence by palpation and ultrasonography. *Arch International Medicine* 1994; 154: 1838 â 1840
6. Strauss L, Conti PS. The application of PET in clinical oncology. *J Nucl Med* 1991; 32: 623 -48
7. Bomanji JB, Costa DC, Ell PJ. Clinical role of positron emission tomography in oncology. *Lancet Oncology* 2001; 2: 157 â 164
8. Cohen MS, Arslan N, Dehdashti F, Doherty GM, Lairmore TC, Brunt LM, Moley JF. Risk of malignancy in thyroid incidentalomas identified by fluorodeoxyglucose-positron emission tomography. *Surgery* 2001; 130: 941 â 946
9. Van der Bruel A, Maes A, De Potter T, Mortelmans L, Drijkoningen M, Van Damme B, Delaere P, Bouillon R. Clinical relevance of thyroid fluorodeoxyglucose-whole body positron emission tomography incidentaloma. *J Clin Endocrinol Metab* 2002; 87: 1517 â 1520
10. Kang KW, Kim SK, Kang HS, Lee ES, Sim JS, Lee IG, Jeong SY, Kim SW. Prevalence and risk of cancer of focal thyroid incidentaloma identified by 18F-fluorodeoxyglucose positron emission tomography for metastasis evaluation and cancer screening in healthy subjects. *J Clin Endocrinol Metab* 2003; 88: 4100 â 4104
11. Kim TY, Kim WB, Ryu JS, Ging G, Hong SJ, Shong YK. 18F-fluorodeoxyglucose uptake in thyroid from positron emission tomogram (PET) for evaluation in cancer patients: high prevalence of malignancy in thyroid incidentaloma. *Laryngoscope* 2005; 115: 1074 â 1078
12. Yi JG, Marom EM, Munden RF, Truong MT, Macapinlac HA, Gladish GW, Sabloff BS, Podoloff DA. Focal uptake of fluorodeoxyglucose by the thyroid in patients undergoing initial disease staging with combined PET/CT for non-small cell lung cancer. *Radiology* 2005; 236: 271 â 275
13. Choi JY, Lee KS, Kim HJ, Shim YM, Kwon OJ, Park K, Baek CH, Chung JH, Lee KH, Kim BT. Focal thyroid lesions incidentally identified by integrated 18F-FDG PET / CT: clinical significance and improved characterization. *J Nucl Med* 2006; 47: 609 â 615
14. Chen W, Parsons M, Torigian DA, Zhuang H, Alavi A. Evaluation of thyroid FDG uptake incidentally identified on FDG-PET/CT imaging. *Nucl Med Communications* 2009; 30: 240 - 244
15. Yasuda S, Shohtsu A, Ide M, Takagi S, Takahashi W, Suzuki Y, Horiuchi M. Chronic thyroiditis: diffuse uptake of FDG at PET. *Radiology* 1998; 207: 775 â 778
16. Wolf G, Aigner RM, Schaffler G, Schwartz T, Krippel P. Pathology results in 18F- fluorodeoxyglucose positron emission tomography of the thyroid gland. *Nucl Med Communications* 2003; 24: 1225 â 1230
17. Rojeski MT, Gharib H. Nodular thyroid disease. Evaluation and management. *N Engl J Med* 1985; 313: 428 â 436
18. Karantanis D, Bogsrud TV, Wiseman GA, Mullan BP, Subramaniam RM, Nathan MA et al. Clinical significance of diffusely increased 18F-FDG uptake in the thyroid gland. *J Nucl Med* 2007; 48: 896 - 901
19. Naklyavani MK, Gharib H, Goellner JR, Van Hearnden JA. Metastasis to the thyroid gland. A report of 43 cases. *Cancer* 1997; 79: 574 - 578
20. Grant CS, Hay ID, Gough IR, McCarthy PM. Long-term follow-up of patients with benign thyroid fine-needle aspiration cytological diagnosis. *Surgery* 1989; 106: 980 - 986