Clinical Thyroidology / Original Paper

European
Thyroid Journal

Eur Thyroid J 2015;4:115–122
DOI: 10.1159/000431319

Received: February 26, 2015
Accepted after revision: May 11, 2015
Published online: June 11, 2015

Incidence and Significance of Incidental Focal Thyroid Uptake on ^{18}F-FDG PET Study in a Large Patient Cohort: Retrospective Single-Centre Experience in the United Kingdom

Kanhaiyalal Agrawal[a] James Weaver[g] Fahim Ul-Hassan[a, f]
Jean-Pierre Jeannon[b] Ricard Simo[b] Paul Carroll[d] Johnathan G. Hubbard[e]
Ashish Chandra[c] Hosahalli Krishnamurthy Mohan[a, f]

Departments of [a]Nuclear Medicine, [b]Otorhinolaryngology Head and Neck Surgery, and [c]Histopathology/Cytology, [d]Consultant Endocrinologist, and [e]Consultant Endocrine Surgeon, Guy's and St Thomas' NHS Foundation Trust, and [f]Clinical PET Centre, King's College London, and [g]King's College London, London, UK

Key Words
Thyroid · Uptake · ^{18}F-FDG · PET

Abstract
Objective: To assess the prevalence and pathological nature of incidental focal thyroid uptake on ^{18}F-FDG (2-[^{18}F]-fluoro-2-deoxy-D-glucose) PET (positron emission tomography) and examine the role of the maximum standardised uptake value (SUV_{max}) to differentiate benign from malignant thyroid pathology. ***Material and Methods:*** ^{18}F-FDG PET reports were retrospectively reviewed. Incidental focal tracer uptake in the thyroid was noted in 147 patients (0.5%). Patients with known primary thyroid malignancy were excluded. The final diagnosis was made following ultrasonography of the neck, fine-needle aspiration cytology (FNAC) or histopathology of the surgically resected specimen where surgery was indicated. A Mann-Whitney U test was used to compare the SUV_{max} of benign and malignant thyroid pathology. Receiver operating characteristic (ROC) analysis was performed to identify an SUV_{max} cutoff in differentiating benign from malignant pathology. ***Results:*** A final diagnosis was achieved in 47/147 (32%) of the patients. The diagnoses included benign lesions in 36 patients and malignancy in 9 patients. In 2 patients, FNAC demonstrated indeterminate follicular lesions; however, surgical excision was not performed. There was a highly significant difference in the mean SUV_{max} of malignant focal thyroid uptake (15.7 ± 5.9) compared to that of benign lesions (7.1 ± 6.8) with a p value of 0.000123. An SUV_{max} of 9.1 achieved a sensitivity of 81.6%, specificity of 100% and area under the curve of 0.915 in the ROC analysis differentiating benign from malignant disease. ***Conclusion:*** The malignancy potential of incidental focal thyroid uptake remains high and warrants prompt and appropriate follow-up by the clinician. The SUV_{max} may aid in further characterisation of the lesion and its management.

KARGER 125

E-Mail karger@karger.com
www.karger.com/etj

2235–0640/15/0042–0115$39.50/0

Dr. Kanhaiyalal Agrawal, MBBS, MD
Department of Nuclear Medicine, Guy's Hospital
Great Maze Pond
London SE19RT (UK)
E-Mail drkanis@gmail.com

Introduction

The prevalence of thyroid nodules in the general population is high and is reported to be between 8 and 65% [1]. Due to the significant advances in imaging technology and the increased use of neck imaging, detection of unsuspected thyroid nodules, known as incidentalomas, is on the rise.

^{18}F-FDG (2-[^{18}F]-fluoro-2-deoxy-D-glucose) PET/CT (positron emission tomography/computed tomography) has been increasingly used for assessment of various malignancies and plays an integral role in cancer management. ^{18}F-FDG is a glucose analogue and the mechanism of ^{18}F-FDG uptake and detection of tumours is based on the higher glycolytic metabolism and the higher expression of membrane glucose transporter (GLUT) proteins in the malignant tissue [2]. Incidental diffuse and focal thyroid uptake is often seen on ^{18}F-FDG PET/CT study. Diffuse uptake in the thyroid has been reported in approximately 0.6–3.3% of the ^{18}F-FDG PET studies and is often due to a benign aetiology [3]. The prevalence of focal uptake within the thyroid (incidentaloma) on ^{18}F-FDG PET has been noted to range from 0.2 to 10.1% in various studies. This is clinically more significant due to its high risk of malignancy in these lesions and the reported risk of malignancy is varied (8–64%) [4]. Malignancy identified within the thyroid incidentaloma on ^{18}F-FDG PET has been noted to be of a higher grade/aggressive subtype [5], requiring prompt evaluation by the clinician. This may create a management dilemma for the referring clinicians [6].

The maximum standardised uptake value (SUV_{max}) assessed by ^{18}F-FDG PET is a semi-quantitative measure of glucose metabolism, which is useful in the estimation of tumour grade or aggressiveness and as a marker in assessment of response to treatment. It is defined as the maximum uptake in the lesion scaled by the administered activity and patient weight or height [7]. Some studies claim a beneficial role of the SUV_{max} in differentiating benign from malignant thyroid pathology, but this has not been replicated in other studies and therefore remains controversial [8, 9].

The aim of this study was to assess the pathological nature of the focal thyroid incidentalomas detected on ^{18}F-FDG PET and the role of the SUV_{max} in differentiation of benign from malignant thyroid pathology in these patients.

Materials and Methods

This was a retrospective study reviewing ^{18}F-FDG PET or PET/CT scan reports of 29,300 studies performed in the nuclear medicine department at our institution between January 1999 and December 2013 for various oncological and non-oncological indications. Institutional review board approval was obtained for the study.

The search criteria 'uptake in the thyroid' was applied to these scan reports, which provided 147 results as having incidental focal tracer uptake in the thyroid. Patients with an established diagnosis of a malignant primary thyroid neoplasm were excluded from the analysis. Data including age, sex, primary malignancy site, indication for the PET study and the SUV_{max} of the focal thyroid uptake were recorded.

PET/CT imaging was performed 60 min after injection of ^{18}F-FDG (5 MBq/kg of body weight). Standard patient preparation prior to the study included a fasting period of at least 4–6 h and a serum glucose level <7 mmol/l (120 mg/dl) before ^{18}F-FDG administration.

The PET scan report in patients with a focal uptake in the thyroid gland recommended further evaluation of the uptake with ultrasonography (USG) with and without fine-needle aspiration (FNA) and where appropriate referral to the head and neck, endocrinology or endocrine surgery teams for further management. The final diagnosis for the focal thyroid incidentalomas was made by USG of the neck, FNA cytology (FNAC) or histopathology of the surgically resected specimen, where available. The prevalence of thyroid incidentalomas on ^{18}F-FDG PET or PET/CT and the rate of malignancy in focal uptake were assessed. The SUV_{max} of focal uptake was noted in patients with a focal thyroid incidentaloma and available final diagnosis.

Statistical Analysis

Statistical analysis was performed using commercially available software package SPSS version 16.0 (SPSS Inc., Chicago, Ill., USA). A Mann-Whitney U test was used to compare the SUV_{max} of benign and malignant thyroid incidentalomas. Statistical significance was defined as $p < 0.05$. Receiver operating characteristic (ROC) analysis was performed to identify an SUV_{max} cutoff in differentiating benign from malignant thyroid incidentalomas.

Results

Incidental focal uptake of tracer in the thyroid was observed in 147 patients. The final diagnosis was achieved in 47/147 (32%) by FNAC in 31 patients, histopathology of the surgical resection specimen in 10 and following neck USG in 6 patients (table 1). In the rest of the patients, final cytological or histopathological diagnosis was not available due to several factors, such as further patient management in other hospitals, advanced primary malignancy with widespread metastatic disease, poor prognosis, low clinical index of suspicion or death. The final diagnosis showed benign lesions in 36 patients, papillary

Table 1. Patient characteristics with focal uptake in the thyroid where a final diagnosis was available

No.	Age, years	Sex	Primary	SUV_{max}	Final diagnosis	Modality for final diagnosis
1	67	F	Breast	7	Benign nodule	FNAC
2	68	F	Breast	3.4	Benign nodule	USG
3	52	F	Colorectal	1.7	Benign nodule	FNAC
4	75	M	Colorectal	3.8	Benign nodule	FNAC
5	72	F	CUPS	14.5	Benign nodule	FNAC
6	68	F	CUPS	2.4	Benign nodule	FNAC
7	46	F	Lymphoma (HL)	1.6	Benign nodule	FNAC
8	59	F	Lung	7.5	Benign nodule	FNAC
9	64	F	Lung	5.8	Benign nodule	FNAC
10	84	M	Lung	2.9	Benign nodule	USG
11	58	F	Lung	5.6	Benign nodule	FNAC
12	65	M	Lung	7.8	Benign nodule	FNAC
13	73	F	Lung	5.9	Benign nodule	Histopathology
14	68	F	Lung	5.4	Benign nodule	Histopathology
15	76	F	Melanoma	6.7	Benign nodule	USG
16	91	F	Melanoma	3.9	Benign nodule	USG
17	46	F	Lymphoma (NHL)	4.9	Benign nodule	FNAC
18	72	F	Lymphoma (NHL)	2.5	Benign nodule	FNAC
19	43	F	Lymphoma (NHL)	3.4	Benign nodule	FNAC
20	84	M	Lymphoma (NHL)	39.0	Benign nodule	FNAC
21	43	F	Lymphoma (NHL)	4.5	Benign nodule	FNAC
22	79	M	Lymphoma (NHL)	4.5	Benign nodule	FNAC
23	35	F	Lymphoma (NHL)	5.0	Benign nodule	FNAC
24	82	F	Lymphoma (NHL)	9.9	Benign nodule	USG
25	53	F	Lymphoma (NHL)	2.1	Benign nodule	Histopathology
26	51	F	Lymphoma (NHL)	10.3	Benign nodule	FNAC
27	71	F	Lymphoma (NHL)	2.5	Benign nodule	FNAC
28	66	M	Lymphoma (NHL)	5	Benign nodule	Histopathology
29	61	M	Oesophagus	9.1	Benign nodule	FNAC
30	48	F	Oesophagus	20.5	Benign nodule	FNAC
31	81	F	SqCC (anterior abdominal wall)	15	Benign nodule	FNAC
32	58	M	SqCC HN	15	Benign nodule	FNAC
33	77	F	Small fibre neuropathy	5.5	Benign nodule	FNAC
34	75	F	Stomach	4.5	Benign nodule	USG
35	47	M	Thymus	4.5	Benign nodule	FNAC
36	81	M	Colorectal	15	Metastases	Histopathology
37	65	M	SqCC HN	9.2	Metastases	FNAC
38	65	F	Lung	10.7	Metastases	FNAC
39	84	M	Lymphoma (NHL), lung	11.5	NHL	FNAC
40	66	F	Lung	15.2	PTC	Histopathology
41	58	M	SPN characterisation	17.4	PTC	Histopathology
42	46	M	Lymphoma – Sézary syndome	15.2	PTC	Histopathology
43	48	F	Lymphoma (NHL)	29.4	PTC	Histopathology
44	49	F	SqCC HN	17.8	PTC	Histopathology
45	65	F	Lung	3.8	THY3	FNAC
46	49	M	Thymoma	8.3	THY3	FNAC
47	37	F	Melanoma	2.1	Thyroiditis	FNAC

CUPS = Carcinoma of unknown primary site; NHL = non-Hodgkins lymphoma; HL = Hodgkins lymphoma; SqCC = squamous cell carcinoma; HN = head and neck; SPN = solitary pulmonary nodule; THY3 = follicular lesion/follicular neoplasm.

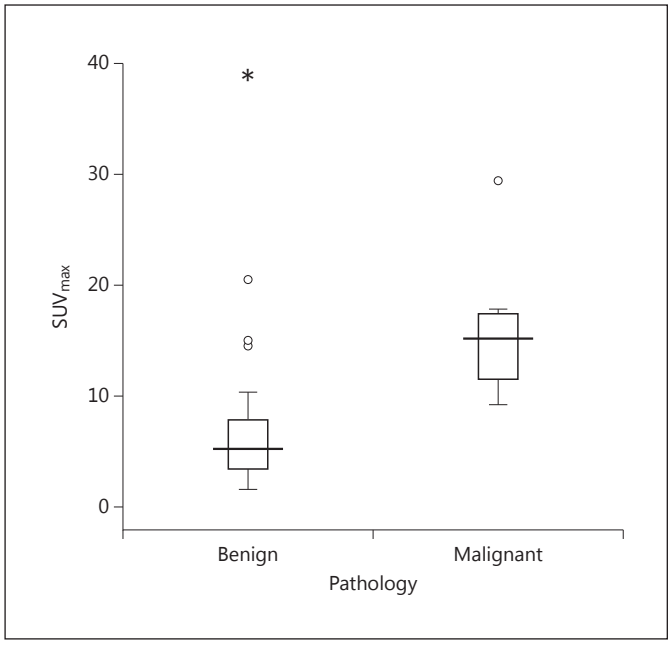


Fig. 1. Box plots of the SUV_{max} of benign and malignant focal incidentalomas.

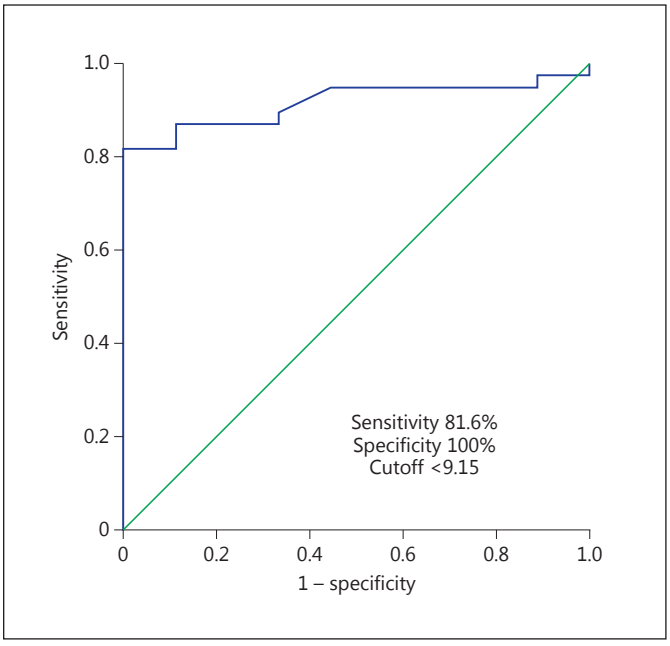


Fig. 2. ROC analysis to identify the cutoff SUV_{max} to differentiate benign from malignant incidentalomas.

thyroid cancer (PTC) in 5 patients (10.6%), secondary metastases in 3 patients and recurrence of lymphoma in 1 patient (table 1). In 2 patients, FNAC demonstrated indeterminate follicular lesions, but surgical excision was not performed. Thus, 9 out of 47 cases (19.1%) of thyroid focal uptake showed malignant involvement. In 5 patients with PTC, completion thyroidectomy histopathology results were available for 3 patients, which showed pT3N1 disease in 2 patients and pT1aN0 disease in 1 patient.

The mean SUV_{max} of malignant focal thyroid uptake was 15.7 ± 5.9 and that of benign lesions was 7.1 ± 6.8. There was a highly significant difference between the SUV_{max} in two groups ($p = 0.000123$; fig. 1). All patients with malignant thyroid pathology had a high SUV_{max} of the focal uptake. Although most of the benign lesions showed low-grade tracer uptake, a high SUV_{max} up to 39.0 was observed.

ROC analysis was performed to identify the cutoff SUV_{max} for differentiating benign from malignant thyroid incidentalomas (fig. 2). The cutoff SUV_{max} identified was 9.1 (sensitivity: 81.6%, specificity: 100%, area under the curve: 0.915). Further, serial ^{18}F-FDG PET studies were performed in 9 out of 47 patients, which showed a stable SUV_{max} over 2–12 months in 5 patients with benign pathology. Two patients had new focal uptake in the thyroid when compared to the previous study, which was confirmed as lymphoma recurrence in one and a benign lesion in the other patient. Other two benign incidentalomas showed a variable trend in the SUV_{max}. Figures 3–5 demonstrate focal thyroid uptake and its significance in a few cases from the study.

Discussion

^{18}F-FDG is a glucose analogue and its mechanism of uptake is based on the higher glycolytic metabolism and the high expression of GLUT proteins in the malignant tissue [2]. The significance of incidental focal thyroid uptake on ^{18}F-FDG PET study was first described in 2001 [10]. Many research studies are currently available on this topic, with different results on focal uptake of tracer on ^{18}F-FDG PET [3–6, 8, 9, 11–38]; however, a large UK series has yet to be reported. We report one of the largest studies on the evaluation of incidental focal ^{18}F-FDG uptake in the thyroid. The largest study by Bertagna et al. [4] included 49,519 patients, and focal thyroid uptake was identified in 1.5% of the patients. The authors reported that 34.1% of incidentalomas were malignant. Two studies with a large patient population by King et al. [26] and Kwak et al. [30] showed very low prevalence of focal in-

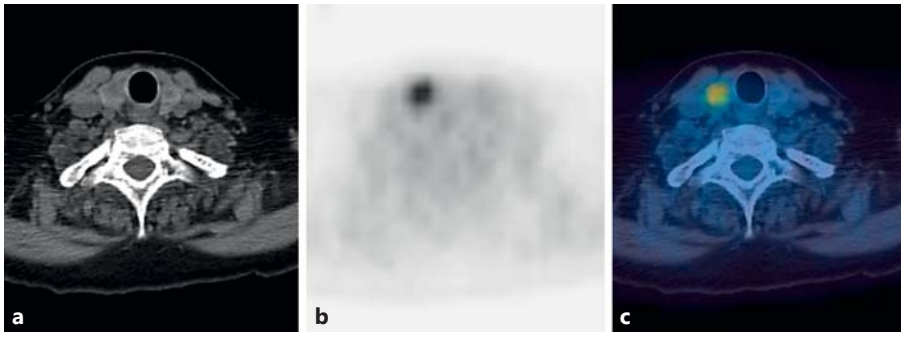


Fig. 3. A 91-year-old-female with previous history of melanoma on ^{18}F-FDG PET/CT study [axial CT (**a**), axial PET (**b**) and fused PET/CT (**c**)] showed incidental focal uptake in the right thyroid lobe with an SUV_{max} of 3.9. On USG evaluation the features of right thyroid lobe nodule were suggestive of benign pathology.

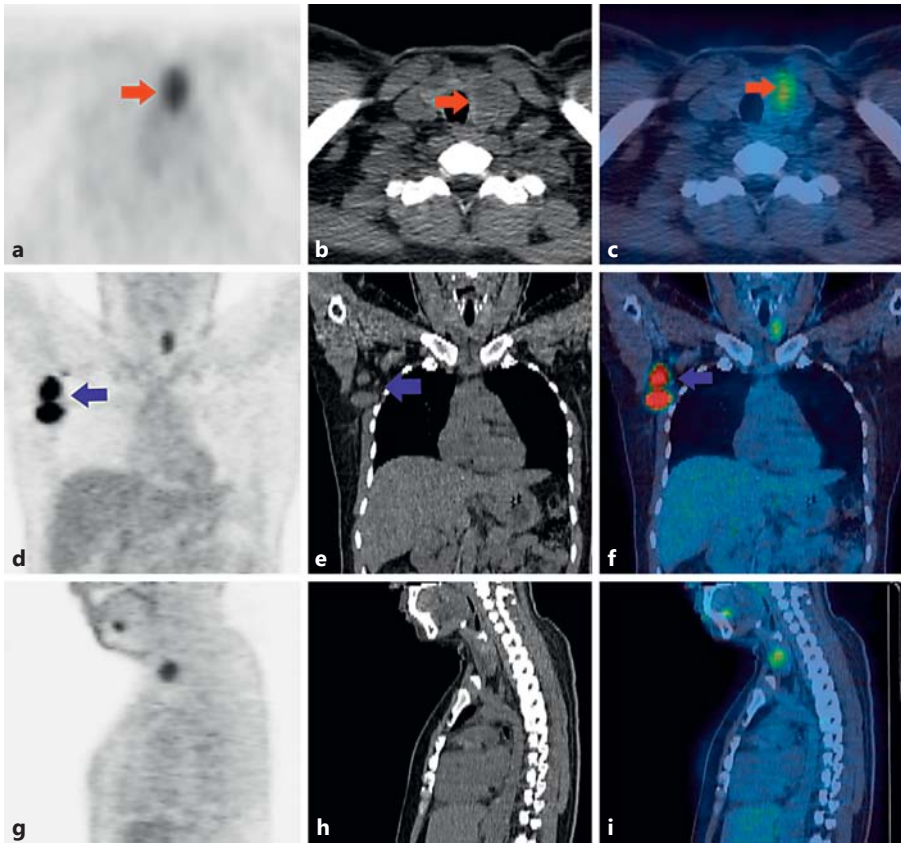
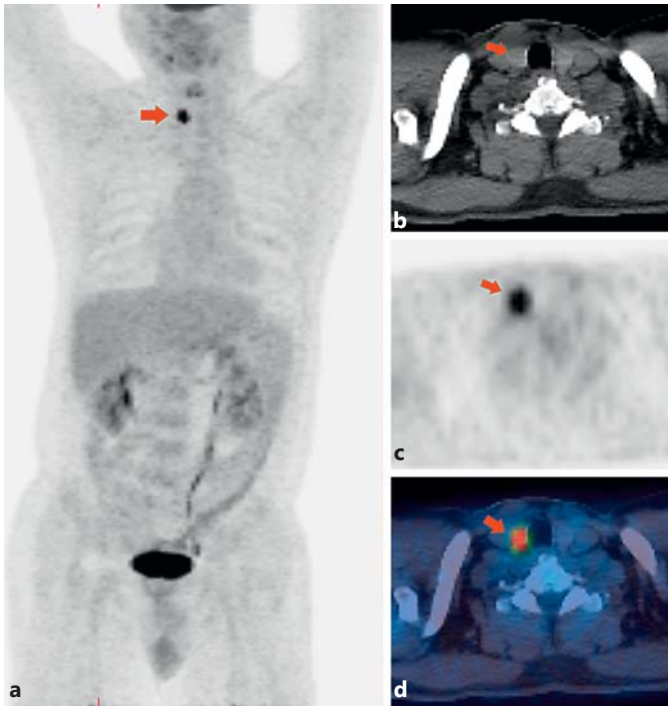


Fig. 4. A 35-year-old-female with high-grade non-Hodgkin's lymphoma on ^{18}F-FDG PET/CT study [axial PET, CT and fused PET/CT (**a–c**); coronal PET, CT and fused PET/CT (**d–f**); sagittal PET, CT and fused PET/CT(**g–i**)] showed incidental focal uptake in a hypodense nodule in the left thyroid lobe (red arrows; colours refer to the online version only) with an SUV_{max} of 5.0. In addition, intense uptake was noted in the right axillary lymph nodes (purple arrows; colours refer to the online version only). On histopathology, the left thyroid nodule was confirmed as a benign follicular adenoma.

cidentalomas in 0.2 and 0.6% of the patients, respectively, similar to our study. However, the prevalence of thyroid incidentalomas on ^{18}F-FDG PET varies from 0.2 to 10.1% in different studies [4]. This could well be related to variation in geographic area, number of patients studied and patient characteristics.

The incidence of malignant neoplasm in our cohort was 19.1% where a final diagnosis was available. Systematic review of previous studies on this topic by Soelberg et al. [39] showed malignancy in 34.8% of patients with focal uptake in the thyroid. However, our study showed a slightly lower incidence of malignant involvement of the thyroid in this population, similar to the King et al. [26] publication.

Previous studies have indicated that PTC and the follicular variant of PTC are the most prevalent thyroid cancer types, accounting for 81.1%, whereas lymphoma and secondary metastatic disease have been seen in only 4.1% of the patients [39]. Our study data is in concordance with previous findings showing PTC as the most frequent his-



Color version available online

Fig. 5. A 58-year-old-male underwent ^{18}F-FDG PET/CT study for assessment of a solitary pulmonary nodule (SPN). ^{18}F-FDG PET/CT showed no uptake in the SPN, but there was intense focal uptake of tracer in a right thyroid lobe nodule [arrow in maximum intensity projection (**a**), axial CT (**b**), axial PET (**c**) and axial fused PET/CT images (**d**)] with an SUV_{max} of 17.4. On histopathology it was confirmed as a PTC.

topathological type of primary thyroid cancer in these patients. Further, we did not find any other histopathological subtypes of the thyroid cancer. It has been mentioned previously that malignancy identified within the thyroid on ^{18}F-FDG PET may be more aggressive, which could be due to the fact that ^{18}F-FDG PET has less sensitivity in identifying differentiated cancers [5]. Interestingly, our results demonstrated that all incidentalomas with primary thyroid malignancies had differentiated PTC, with 1 patient having pT1a disease. FDG avid lesions are likely to be those that express GLUT1 intensely. There is some evidence that phosphatase and tensin homologue (PTEN)-negative PTC have considerable GLUT1 expression, and the relationship between the increasingly understood genetic alterations (BRAF, PTEN, etc.) and FDG avidity merits further study [40]. Furthermore, contradicting the previous findings, we found that almost half (44.4%) of the patients with malignant incidentaloma were due to secondary metastases or lymphoma.

The SUV assessed by ^{18}F-FDG PET/CT is a semiquantitative measure of glucose metabolism, which often reflects metabolic activity frequently correlated with biologic aggressiveness and clinical behaviour of malignant lesions, though not specific for malignancy. Literature evidence on the SUV_{max} in benign and malignant lesions vary with several reports showing a statistically significant difference [9, 13, 19, 21–23, 34, 41] whilst many others have shown no significant difference [8, 14, 15, 27, 30, 32, 33, 35, 36]. Previous studies have also reported cutoff SUV values ranging from 3.5 to 5 in differentiated benign to malignant thyroid lesions [24, 34, 41]. In our study, a highly statistical difference was present between the SUV_{max} of benign and malignant lesions. We found a cutoff value of 9.1 had 81.6% sensitivity and 100% specificity in differentiating benign from malignant lesions.

Considering the literature evidence and following the findings from our study, it may be suggested that in patients with an incidental focal thyroid uptake, an SUV_{max} <3.3 and low clinical risk, one may be able to reassure the patients [42]. However, if there is a high clinical risk (such as previous history of radiation exposure and family history of thyroid cancer) or if the SUV_{max} is higher, the thyroid uptake should be regarded as suspicious for underlying malignancy and investigated further as appropriate. However, in patients with widespread metastases with poor prognosis, further investigation of incidental thyroid uptake may not be appropriate. The decision regarding investigating the incidental thyroid uptake needs to be made on an individual patient basis.

There are some limitations to our study which need to be mentioned. This being a retrospective study, a definitive diagnosis could not be available in many patients due to reasons such as further patient management in other hospitals, advanced primary malignancy with widespread metastatic disease, poor prognosis, low clinical index of suspicion or death. As data was collected over nearly 14 years, the studies were performed on different PET or PET/CT scanners. To our knowledge, however, this is the largest UK series on thyroid incidentalomas over the past 14 years. The results of this study are important as a lot of these findings were determined in a cohort of patients with poor prognosis or who may be terminally ill. It is also essential that patients with incidental focal thyroid uptake are properly evaluated and a collaborative protocol is established between referring clinicians, nuclear medicine physicians, endocrinologists and thyroid surgeons for the appropriate management of these patients.

Conclusion

Incidence of focal thyroid uptake on ^{18}F-FDG PET study remains rare in our study cohort. The malignancy potential of these lesions, however, remains high and warrants prompt follow-up by the clinician. The SUV_{max} may aid in further characterisation of the lesion and its management. Incidence of malignant primary and secondary pathology within these lesions remains equally possible.

Disclosure Statement

The authors declare that they have no conflicts of interest.

References

1 Dean DS, Gharib H: Epidemiology of thyroid nodules. Best Pract Res Clin Endocrinol Metab 2008;22:901–911.
2 Wahl RL: Targeting glucose transporters for tumor imaging: 'sweet' idea, 'sour' result. J Nucl Med 1996;37:1038–1041.
3 Yiyan Liu: Clinical significance of thyroid uptake on F18-fluorodeoxyglucose positron emission tomography. Ann Nucl Med 2009; 23:17–23.
4 Bertagna F, Treglia G, Piccardo A, Giovannini E, Bosio G, Biasiotto G, Bahij el K, Maroldi R, Giubbini R: F18-FDG PET/CT thyroid incidentalomas: a wide retrospective analysis in three Italian centres on the significance of focal uptake and SUV value. Endocrine 2013;43:678–685.
5 Are C, Hsu JF, Ghossein RA, Schoder H, Shah JP, Shaha AR: Histological aggressiveness of fluorodeoxyglucose positron-emission tomogram (FDG-PET)-detected incidental thyroid carcinomas. Ann Surg Oncol 2007;14:3210–3215.
6 Prichard RS, Cotter M, Evoy D, Gibbons D, Collins C, McDermott E, Skehan S: Focal thyroid incidentalomas identified with whole-body FDG-PET warrant further investigation. Ir Med J 2011;104:177–179.
7 Visser EP, Boerman OC, Oyen WJ: SUV: from silly useless value to smart uptake value. J Nucl Med 2010;51:173–175.
8 Are C, Hsu JF, Schoder H, Shah JP, Larson SM, Shaha AR: FDG-PET detected thyroid incidentalomas: need for further investigation? Ann Surg Oncol 2007;14:239–247.
9 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: 941–946.
10 Ramos CD, Chisin R, Yeung HW, Larson SM, Macapinlac HA: Incidental focal thyroid uptake on FDG positron emission tomographic scans may represent a second primary tumor. Clin Nucl Med 2001;26:193–197.
11 Salvatori M, Melis L, Castaldi P, Maussier ML, Rufini V, Perotti G, Rubello D: Clinical significance of focal and diffuse thyroid diseases identified by ^{18}F-fluorodeoxyglucose positron emission tomography. Biomed Pharmacother 2007;61:488–493.
12 Chen YK, Ding HJ, Chen KT, Chen YL, Liao AC, Shen YY, Su CT, Kao CH: Prevalence and risk of cancer of focal thyroid incidentaloma identified by ^{18}F-fluorodeoxyglucose positron emission tomography for cancer screening in healthy subjects. Anticancer Res 2005; 25:1421–1426.
13 Choi JY, Lee KS, Kim HJ, Shim YM, Kwon OJ, Park K, Baek CH, Chung JH, Lee K, Kim BT: Focal thyroid lesions incidentally identified by integrated ^{18}F-FDG PET/CT: clinical significance and improved characterization. J Nucl Med 2006;47:609–615.
14 Kim TY, Kim WB, Ryu JS, Gong G, Hong SJ, Shong YK: ^{18}F-fluorodeoxyglucose uptake in thyroid from positron emission tomogram (PET) for evaluation in cancer patients: high prevalence of malignancy in thyroid PET incidentaloma. Laryngoscope 2005;115:1074–1078.
15 Bogsrud TV, Karantanis D, Nathan MA, Mullan BP, Wiseman GA, Collins DA, Kasperbauer JL, Strome SE, Reading CC, Hay ID, Lowe VJ: The value of quantifying ^{18}F-FDG uptake in thyroid nodules found incidentally on whole-body PET-CT. Nucl Med Commun 2007;28:373–381.
16 Chu QD, Connor MS, Lilien DL, Johnson LW, Turnage RH, Li BD: Positron emission tomography (PET) positive thyroid incidentaloma: the risk of malignancy observed in a tertiary referral center. Am Surg 2006;72: 272–275.
17 Nishimori H, Tabah R, Hickeson M, How J: Incidental thyroid 'PETomas': clinical significance and novel description of the self-resolving variant of focal FDG-PET thyroid uptake. Can J Surg 2011;54:83–88.
18 Ishimori T, Patel PV, Wahl RL: Detection of unexpected additional primary malignancies with PET/CT. J Nucl Med 2005;46:752–757.
19 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 ^{18}F-fluorodeoxyglucose positron emission tomography for metastasis evaluation and cancer screening in healthy subjects. J Clin Endocrinol Metab 2003;88:4100–4104.
20 Nilsson IL, Arnberg F, Zedenius J, Sundin A: Thyroid incidentaloma detected by fluorodeoxyglucose positron emission tomography/computed tomography: practical management algorithm. World J Surg 2011;35:2691–2697.
21 Ho TY, Liou MJ, Lin KJ, Yen TC: Prevalence and significance of thyroid uptake detected by ^{18}F-FDG PET. Endocrine 2011;40:297–302.
22 Kim BH, Na MA, Kim IJ, Kim SJ, Kim YK: Risk stratification and prediction of cancer of focal thyroid fluorodeoxyglucose uptake during cancer evaluation. Ann Nucl Med 2010; 24:721–728.
23 Pagano L, Sama MT, Morani F, Prodam F, Rudoni M, Boldorini R, Valente G, Marzullo P, Baldelli R, Appetecchia M, Isidoro C, Aimaretti G: Thyroid incidentaloma identified by ^{18}F-fluorodeoxyglucose positron emission tomography with CT (FDG-PET/CT): clinical and pathological relevance. Clin Endocrinol (Oxf) 2011;75:528–534.
24 Bae JS, Chae BJ, Park WC, Kim JS, Kim SH, Jung SS, Song BJ: Incidental thyroid lesions detected by FDG-PET/CT: prevalence and risk of thyroid cancer. World J Surg Oncol 2009;7:63.
25 Zhai G, Zhang M, Xu H, Zhu C, Li B: The role of ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography whole body imaging in the evaluation of focal thyroid incidentaloma. J Endocrinol Invest 2010; 33:151–155.
26 King DL, Stack BC Jr, Spring PM, Walker R, Bodenner DL: Incidence of thyroid carcinoma in fluorodeoxyglucose positron emission tomography-positive thyroid incidentalomas. Otolaryngol Head Neck Surg 2007;137: 400–404.
27 Nam SY, Roh JL, Kim JS, Lee JH, Choi SH, Kim SY: Focal uptake of ^{18}F-fluorodeoxyglucose by thyroid in patients with nonthyroidal head and neck cancers. Clin Endocrinol (Oxf) 2007;67:135–139.
28 Even-Sapir E, Lerman H, Gutman M, Lievshitz G, Zuriel L, Polliack A, Inbar M, Metser U: The presentation of malignant tumours and pre-malignant lesions incidentally found on PET-CT. Eur J Nucl Med Mol Imaging 2006;33:541–552.

29 Ohba K, Nishizawa S, Matsushita A, Inubushi M, Nagayama K, Iwaki H, Matsunaga H, Suzuki S, Sasaki S, Oki Y, Okada H, Nakamura H: High incidence of thyroid cancer in focal thyroid incidentaloma detected by ^{18}F-fluorodeoxyglucose [corrected] positron emission tomography in relatively young healthy subjects: results of 3-year follow-up. Endocr J 2010;57:395–401.
30 Kwak JY, Kim EK, Yun M, Cho A, Kim MJ, Son EJ, Oh KK: Thyroid incidentalomas identified by ^{18}F-FDG PET: sonographic correlation. AJR Am J Roentgenol 2008;191:598–603.
31 Hsieh H, Lin S, Yang B, Chu Y, Chang C, Liu R: The clinical relevance of thyroid incidentalomas detected by ^{18}F-fluorodeoxyglucose positron emission tomography. Ann Nucl Med Sci 2003;16:53–58.
32 Chen W, Parsons M, Torigian DA, Zhuang H, Alavi A: Evaluation of thyroid FDG uptake incidentally identified on FDG-PET/CT imaging. Nucl Med Commun 2009;30:240–244.
33 Eloy JA, Brett EM, Fatterpekar GM, Kostakoglu L, Som PM, Desai SC, Genden EM: The significance and management of incidental [^{18}F]fluorodeoxyglucose-positron-emission tomography uptake in the thyroid gland in patients with cancer. AJNR Am J Neuroradiol 2009;30:1431–1434.
34 Kang BJ, Hyun J, Baik JH, Jung SL, Park YH, Chung SK: Incidental thyroid uptake on F-18 FDG PET/CT: correlation with ultrasound and pathology. Ann Nucl Med 2009;23:729–737.
35 Bonabi S, Schmidt F, Broglie MA, Haile SR, Stoeckli SJ: Thyroid incidentalomas in FDG-PET/CT: prevalence and clinical impact. Eur Arch Otorhinolaryngol 2012;269:2555–2560.
36 Pampaloni MH, Win AZ: Prevalence and characteristics of incidentalomas discovered by whole body FDG PETCT. Int J Mol Imaging 2012;2012:476763.
37 Lee WM, Kim BJ, Kim MH, Choi SC, Ryu SY, Lim I, Kim K: Characteristics of thyroid incidentalomas detected by pre-treatment [F]FDG PET or PET/CT in patients with cervical cancer. J Gynecol Oncol 2012;23:43–47.
38 Kim H, Kim SJ, Kim IJ, Kim K: Thyroid incidentalomas on FDG PET/CT in patients with non-thyroid cancer – a large retrospective monocentric study. Onkologie 2013;36:260–264.
39 Soelberg KK, Bonnema SJ, Brix TH, Hegedüs L: Risk of malignancy in thyroid incidentalomas detected by ^{18}F-fluorodeoxyglucose positron emission tomography: a systematic review. Thyroid 2012;22:918–925.
40 Morani F, Pagano L, Prodam F, Aimaretti G, Isidoro C: Loss of expression of the oncosuppressor PTEN in thyroid incidentalomas associates with GLUT1 plasma membrane expression. Panminerva Med 2012;54:59–63.
41 Boeckmann J, Bartel T, Siegel E, Bodenner D, Stack BC Jr: Can the pathology of a thyroid nodule be determined by positron emission tomography uptake? Otolaryngol Head Neck Surg 2012;146:906–912.
42 Qu N, Zhang L, Lu ZW, Wei WJ, Zhang Y, Ji QH: Risk of malignancy in focal thyroid lesions identified by ^{18}F-fluorodeoxyglucose positron emission tomography or positron emission tomography/computed tomography: evidence from a large series of studies. Tumour Biol 2014;35:6139–6147.