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**ORIGINAL ARTICLE**

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# **Incidence and Clinical Impact of Focal Pituitary Uptake in <sup>18</sup>F-Fluorodeoxyglucose Positron-emission Tomography–Computed Tomography: 5-Year Retrospective Review**

**KK Wu, BT Kung, TK Au Yong**

*Nuclear Medicine Unit, Queen Elizabeth Hospital, Jordan, Hong Kong*

## **ABSTRACT**

**Objectives:** To identify the incidence and clinical significance of incidental pituitary uptake in whole-body positron-emission tomography–computed tomography using <sup>18</sup>F-fluoro-2-deoxy-D-glucose (<sup>18</sup>F-FDG PET-CT) in Hong Kong.

**Methods:** We retrospectively reviewed 14,438 records from patients for whom <sup>18</sup>F-FDG PET-CT was performed at a public general hospital from 1 September 2007 to 31 August 2012. Patients with known pituitary pathology were excluded. The final diagnosis was based on brain magnetic resonance imaging (MRI) and enhanced CT with or without hormonal assay. Patients with or without an identified pituitary lesion were assigned to the incidentaloma group or the physiological group, respectively. Non-parametric statistical testing and receiver operating characteristic curve analysis were performed to examine data from the two groups. An optimal cut-off maximum standardised uptake value (SUVmax) value was determined to differentiate physiological uptake from other causes.

**Results:** Incidental pituitary uptake was identified in 55 of 14,438 cases (incidence, 0.38%). After MRI or enhanced CT was performed in 25 of 55 cases, 11 were assigned to the incidentaloma group and the remaining 14 as the physiological group. There was a generally higher SUVmax value in the incidentaloma group (median, 7.30; range, 4.50-17.30) than in the physiological group (median, 3.45; range, 2.60-5.80). The optimal diagnostic cut-off value to discriminate between the two groups was an SUVmax of 4.30 (sensitivity = 100%; specificity = 92.9%; area under the curve = 0.987).

**Conclusions:** Incidental pituitary uptake is a rare finding in <sup>18</sup>F-FDG PET-CT. A high SUVmax value is associated with an increased probability of pituitary incidentaloma and indicates that further imaging and hormonal evaluation are warranted.

**Key Words:** Fluorodeoxyglucose F18; Pituitary gland; Positron-emission tomography

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**Correspondence:** Dr KK Wu, Nuclear Medicine Unit, LG, Block K, Queen Elizabeth Hospital, Jordan, Kowloon, Hong Kong.  
Email: kksamwu@gmail.com

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## 中文摘要

### <sup>18</sup>F-FDG PET-CT 檢查出現垂體局部攝取的發生率及其臨床意義： 五年追溯性回顧

胡君傑、龔本霆、歐陽定勤

**目的：**探討<sup>18</sup>F-FDG PET-CT全身檢查診斷偶發垂體攝取的發生率及其臨床意義。

**方法：**回顧分析2007年9月1日至2012年8月31日期間在香港一所公立醫院的14,438例<sup>18</sup>F-FDG PET-CT檢查報告，並排除已知垂體有病理改變的受試者。最後診斷基於腦MRI和增強CT或者結合激素評估。出現垂體病灶的受試者納入偶發瘤組，沒有病灶的則納入生理學組。兩組數據以非參數測試和ROC曲線分析，並確定最佳SUVmax閾值（即病灶最大標準化攝取值）以區別生理攝取與其他原因。

**結果：**在14,438例中有55例偶發垂體攝取（發生率0.38%）。55名受試者中有25名進行MRI或增強CT檢查，當中11名被納入偶發瘤組，其餘14名在生理學組。偶發瘤組的SUVmax閾值（中位數7.30，範圍4.50-17.30）較生理學組高（中位數3.45，範圍2.60-5.80）。區分兩組的最佳診斷截止值（SUVmax閾值）為4.30（靈敏度100%、特異性92.9%、ROC曲線下面積0.987）。

**結論：**經<sup>18</sup>F-FDG PET-CT檢查發現偶發垂體攝取屬罕見。高SUVmax閾值增加垂體偶發瘤的可能性，所以進一步影像學檢查和激素評估是必要的。

## INTRODUCTION

Whole-body positron-emission tomography-computed tomography (PET-CT) using <sup>18</sup>F-fluoro-2-deoxy-D-glucose (<sup>18</sup>F-FDG) plays a vital role in current clinical practice and is increasingly performed for various indications. Its increased use also leads to an increased detection of incidental pituitary lesions in clinical practice. Several case reports have described the incidental finding of pituitary <sup>18</sup>F-FDG uptake in various conditions, including pituitary adenoma, pituitary carcinoma, lymphoma, and hypophysitis.<sup>1-7</sup> However, few studies have reported on the clinical significance of incidentally detected pituitary <sup>18</sup>F-FDG uptake and the criterion for differentiating pathological from physiological pituitary uptake.<sup>8,9</sup> To date, the occurrence and significance of incidental pituitary uptake in <sup>18</sup>F-FDG PET-CT in Hong Kong has not yet been reported.

This study aimed to identify the incidence and clinical impact of incidental pituitary uptake in whole-body <sup>18</sup>F-FDG PET-CT at a single centre at a public general hospital in Hong Kong over a 5-year period. Additionally, we assessed the value of a semi-quantitative variable of FDG uptake in discriminating pathological and physiological pituitary uptake.

## METHODS

### Patient Population

This study was approved by the local institutional review board. We retrospectively studied 14,438 clinical records from consecutive patients who had undergone <sup>18</sup>F-FDG PET-CT from 1 September 2007 to 31 August 2012 at the Queen Elizabeth Hospital, Hong Kong. Patients with increased pituitary uptake who then underwent correlative magnetic resonance imaging (MRI) or contrast CT were included in this study. Among this population, patients with previous known pituitary or sella pathology (such as invasion from nasopharyngeal carcinoma) were excluded. Patient history, laboratory test results, and drug history were reviewed.

### Imaging Acquisition and Analysis

All patients fasted for at least 6 hours before the PET-CT study. Whole-body PET-CT was initiated 60 minutes after intravenous injection of 370 MBq of <sup>18</sup>F-FDG. Images were obtained from the vertex to the proximal thigh using the PET-CT scanner (Discovery LS; GE Healthcare, USA) with a spatial resolution of 6.6 mm in the centre of the field of view. Image acquisition was performed with 3 minutes per bed position. Low-dose CT was performed for attenuation correction and

lesion localisation. No intravenous contrast agent was administered. The obtained data were reconstructed using an iterative ordered-subset expectation maximisation algorithm. A Z-axis filter was used and a total of two iterations were performed.

The intensity of <sup>18</sup>F-FDG uptake was semi-quantitatively measured as the maximum standardised uptake value (SUVmax) after normalisation to bodyweight using the following equation:  $SUV = A / (ID / BW)$ , where A represents the decay and attenuation-corrected activity in tissue (MBq/mL), ID represents the injected dose of <sup>18</sup>F-FDG (MBq), and BW represents bodyweight (g).

### Statistical Analysis

Patients were assigned to the incidentaloma group or physiological group on the basis of corresponding contrast CT or MRI findings, with or without information from hormonal assays. Differences between the two groups were assessed by the non-parametric Mann-Whitney *U* test. Statistical significance was assumed for *p* values of <0.05. Receiver operating characteristic (ROC) curve analysis was performed to determine an optimal cut-off value for SUVmax for differentiating pathological from physiological uptake. Statistical analysis was performed using SPSS (Windows version 15.0; SPSS Inc., Chicago [IL], USA).

### RESULTS

Increased pituitary <sup>18</sup>F-FDG uptake was an incidental finding on PET-CT for 55 of 14,438 cases (incidence, 0.38%), involving 47 patients. Of the 55 cases of pituitary uptake, 25 cases (involving 22 patients) also had correlative MRI (*n* = 22) or contrast CT (*n* = 3) performed as part of their investigations for malignancy (*n* = 24) and for pyrexia (*n* = 1) [Table]. Eleven cases were classified as the incidentaloma group (10 by MRI and one by contrast CT), and 14 were classified as the physiological group (12 by MRI and two by contrast CT). In the incidentaloma group, lesions identified included microadenoma (*n* = 2; Figure 1), macroadenoma (*n* = 2), and nodules of an indeterminate nature (*n* = 7).

An outlier case (case 23) was observed in the physiological group with a pituitary SUVmax of 5.8 and thyroid SUVmax of 5.3 (Figure 2). This patient had unremarkable MRI findings at the pituitary fossa, but an elevated level of thyroid-stimulating hormone (159 mIU/L). The pituitary hormonal profile was otherwise unremarkable and a diagnosis was made of primary

hypothyroidism.

The median pituitary SUVmax was 7.30 (range, 4.50-17.30) for the incidentaloma group and 3.45 (range, 2.60-5.80) for the physiological group. Excluding the outliers, the median pituitary SUVmax was 7.30 (range, 4.50-11.90) for the incidentaloma group and 3.40 (range, 2.60-4.10) for the physiological group. The pituitary SUVmax of the incidentaloma group was significantly higher than that of the physiological group (*p* < 0.001; Figure 3). According to ROC analysis, the optimal diagnostic cut-off value to discriminate between the incidentaloma and physiological groups was an SUVmax of 4.30 (sensitivity = 100%; specificity = 92.9%; area under the curve = 0.987).

### DISCUSSION

The pituitary fossa is now commonly included in routine whole-body PET-CT imaging, but knowledge about the significance of an incidental finding of increased pituitary FDG uptake is limited. Existing evidence is limited to case reports and two retrospective studies.<sup>1-9</sup> In our study, most cases of incidental increased pituitary FDG uptake did not have subsequent correlative MRI or contrast CT performed (30 of 55 cases, or 25 of 47 patients). The reason is likely due to the advanced stage of metastatic disease in those cases, precluding further investigation for the pituitary lesion. The reported incidence of incidental increased pituitary FDG uptake in two retrospective studies<sup>8,9</sup> was 0.073% and 0.8%. In our study, the incidence was 0.38%. The discrepancy in the three values may be related to variation in the reporting threshold of pituitary FDG uptake.

Multiple case reports have described incidental increased pituitary FDG uptake in various conditions. De Souza et al<sup>1</sup> reported that 12 of 20 surgically verified pituitary microadenoma showed a positive FDG PET finding, whereas none of the 20 healthy controls showed a false-positive result. Koo et al<sup>2</sup> reported a case of growth hormone-secreting pituitary macroadenoma with intense FDG uptake. Soussan et al<sup>3</sup> and Campeau et al<sup>4</sup> reported cases of non-Hodgkin's lymphoma involving the pituitary fossa that presented as intense pituitary FDG uptake. Van der Hiel et al<sup>5</sup> reported a case of ipilimumab-induced hypophysitis that presented as incidental pituitary hypermetabolism in FDG PET-CT.

A retrospective study by Jeong et al<sup>9</sup> reported that 18 of 19 subjects (95%) with incidental increased

**Table.** Clinical findings for patients with incidental pituitary fluorodeoxyglucose uptake on PET-CT.

Case	Sex	Indication	Pituitary SUVmax	MRI	Contrast CT	Hormonal profile	Group	Remarks
1	M	CA lung	8.3	+	NA	NA	Incidentaloma	0.9-cm microadenoma
2	F	CA lung	3.1	-	NA	NA	Physiological	
3	M	Renal cell carcinoma	7.9	+	NA	-	Incidentaloma	1.0-cm pituitary adenoma or metastasis
4	F	CA breast	3.0	-	NA	NA	Physiological	
5	M	Brain tumour	4.1	-	NA	NA	Physiological	
6*	F	CA breast	3.7	-	NA	NA	Physiological	
7*	F	CA breast	3.5	-	NA	NA	Physiological	
8	M	CA colon	11.9	+	NA	+	Incidentaloma	1.2-cm pituitary adenoma or metastasis
9	F	Renal cell carcinoma	7.1	+	NA	+	Incidentaloma	Biopsy: ACTH secreting macroadenoma
10	F	CA colon	17.3	+	NA	-	Incidentaloma	Enlarged anterior pituitary gland Imp: adenoma or metastasis
11	M	CA colon	3.1	NA	-	NA	Physiological	
12	F	CA lung	3.2	-	NA	NA	Physiological	
13	F	PUO	3.4	-	NA	-	Physiological	
14	F	NPC	4.0	-	NA	NA	Physiological	
15†	M	Gastric GIST	4.5	+	NA	-	Incidentaloma	7-mm pituitary nodule
16†	M	Gastric GIST	6.2	+	NA	-	Incidentaloma	7-mm pituitary nodule
17†	M	Gastric GIST	5.6	+	NA	-	Incidentaloma	7-mm pituitary nodule
18	M	NPC	4.1	-	NA	-	Physiological	
19	M	Liposarcoma	3.8	-	NA	-	Physiological	
20	F	CA lung	3.1	NA	-	NA	Physiological	
21	M	CA colon	7.3	+	NA	NA	Incidentaloma	1.1-cm pituitary nodule
22	F	CA breast	7.3	NA	+	+	Incidentaloma	0.7-cm pituitary nodule; elevated prolactin >3000
23	F	NPC	5.8	-	NA	+	Physiological	Elevated TSH 159 (later confirmed primary hypothyroidism); other hormone normal
24	F	CA breast	2.6	-	NA	-	Physiological	
25	F	Vaginal clear cell CA	11.8	+	NA	-	Incidentaloma	1.9-cm macroadenoma

Abbreviations: + = positive finding; - = normal finding; ACTH = adrenocorticotrophic hormone; CA = carcinoma; FDG = fluorodeoxyglucose; GIST = gastrointestinal stromal tumour; MRI = magnetic resonance imaging; NA = not available; NPC = nasopharyngeal carcinoma; PET-CT = positron-emission tomography-computed tomography; PUO = pyrexia of unknown origin; SUVmax = maximum standardised uptake value; TSH = thyroid-stimulating hormone.

\* Cases 6-7 were the same patient.

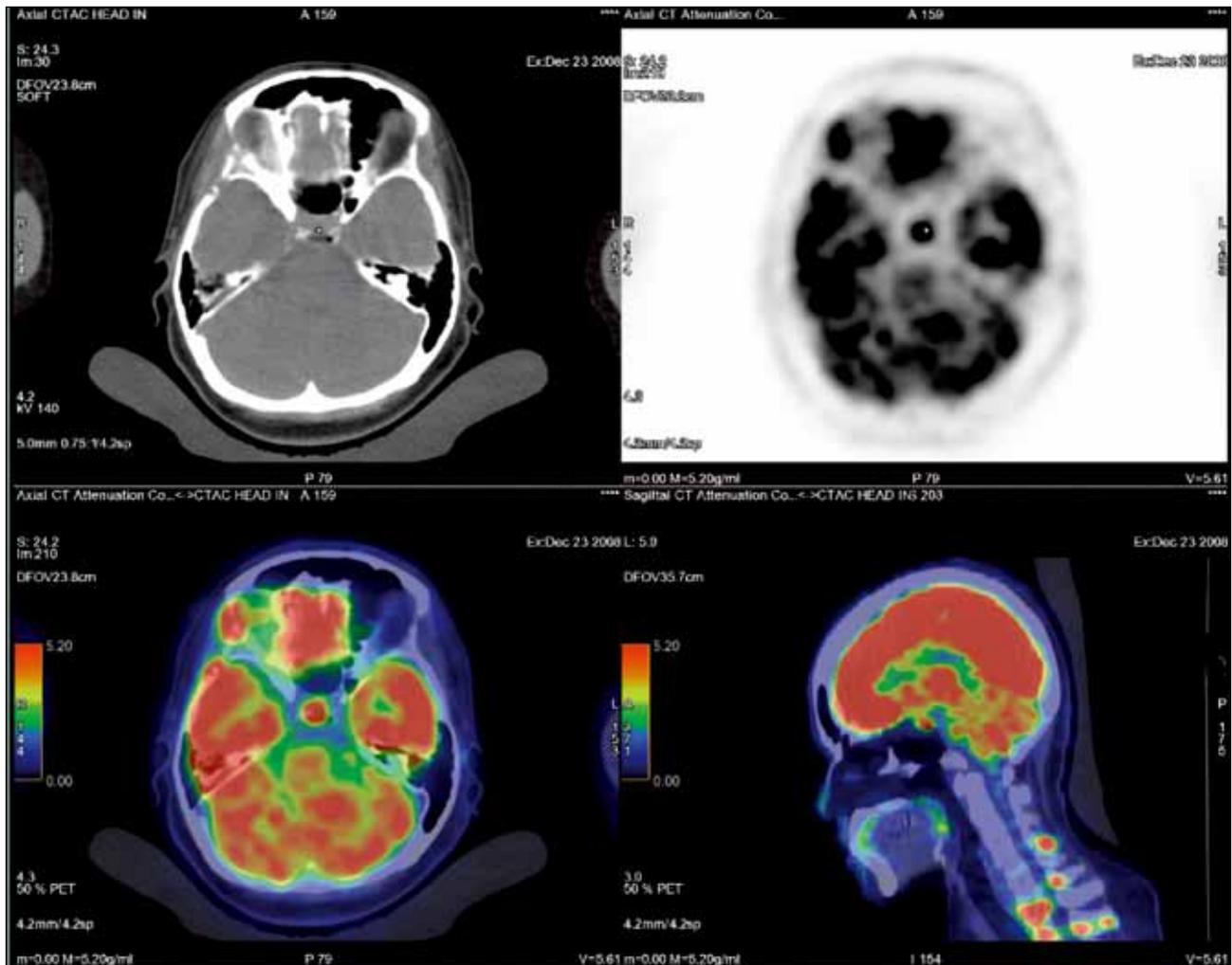
† Cases 15-17 were the same patient.

pituitary FDG uptake had abnormal MRI findings that were suggestive of a pituitary lesion. They found that macroadenomas had a higher FDG uptake than microadenomas, but there was no statistically significant difference in the SUVmax of pituitary lesions with or without pituitary hormone hypersecretion. Another retrospective study, by Hyun et al,<sup>8</sup> reported a statistically significant difference for intensity of FDG uptake between pathological and physiological uptake, with a cut-off SUVmax of 4.1 showing a sensitivity of 96.6% and specificity of 88.1%. Those findings are similar to those of our study for an SUVmax cut-off value of 4.3—namely, high sensitivity (100%), and specificity (92.9%).

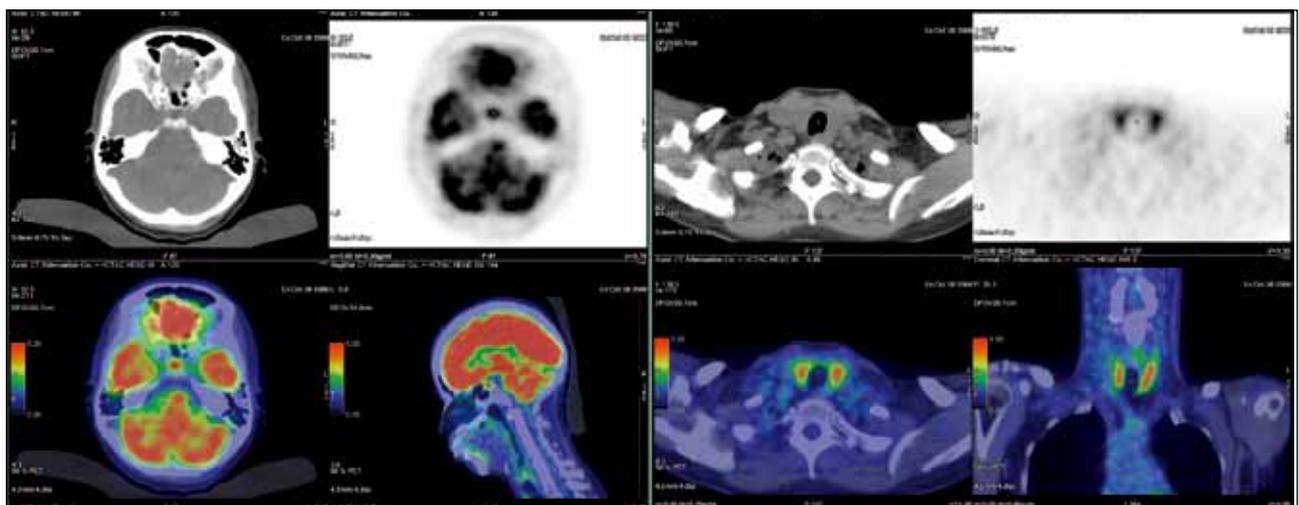
In our study, the outlier case in the physiological group

had an SUVmax of 5.8 and was eventually diagnosed as primary hypothyroidism. A study by Jeong et al<sup>10</sup> revealed a strong positive correlation between pituitary FDG uptake and serum thyroid-stimulating hormone in 44 patients with diffuse thyroid FDG uptake. We postulate that the high pituitary FDG uptake of our outlier patient in the physiological group might be secondary to the underlying primary hypothyroidism. After excluding this outlier case, the cut-off value of SUVmax 4.3 was able to discriminate the incidentaloma group and physiological group with a sensitivity and specificity of 100%.

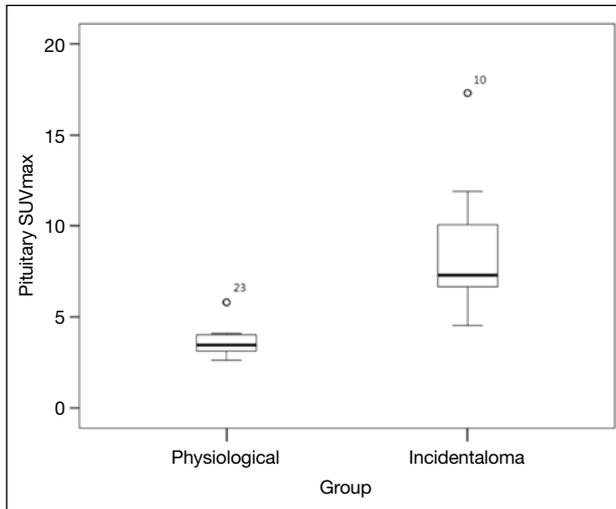
There are two main limitations in our study. First, histological diagnosis was available in only one patient and hormonal assays were not performed in all included



**Figure 1.** A case of incidental increased pituitary fluorodeoxyglucose uptake (case 22; maximum standardised uptake value, 7.3). Magnetic resonance imaging and hormonal assay suggested prolactin-secreting pituitary microadenoma.



**Figure 2.** The outlier case (case 23) in the physiological group, with increased pituitary fluorodeoxyglucose uptake (maximum standardised uptake value, 5.8) and diffuse mildly increased thyroid uptake (maximum standardised uptake value, 5.3).



**Figure 3.** Distribution of pituitary maximum standardised uptake value (SUVmax) in the physiological and incidentaloma groups, showing median (range) SUVmax of 3.40 (2.60-4.10) and 7.30 (4.50-11.90), respectively after excluding the outliers.

subjects. Second, our study was a retrospective review of PET-CT reports that had been written by multiple nuclear medicine physicians; hence, inter-reader variations in reporting were expected.

## CONCLUSION

An incidental finding of increased pituitary uptake in  $^{18}\text{F}$ -FDG PET-CT is rare. A high pituitary SUVmax value is associated with an increased probability of

pituitary incidentaloma and indicates that further imaging and hormonal evaluation are warranted.

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