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# Incidental Pituitary FDG Uptake on PET-CT: A Retrospective Review of Current Practice and Outcomes at a UK Tertiary Centre

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## ABSTRACT

**Context:** Fluorine-18 fluorodeoxyglucose (FDG) positron emission tomography-computed tomography (PET-CT) is widely used in malignancy diagnosis and surveillance. However, benign conditions also increase avidity. Distinguishing between benign and pathological uptake is critical. Rising PET-CT utilisation has led to increased detection of incidental pituitary FDG uptake. Referral pathways and secondary imaging remain inconsistent, and no UK guidelines exist. This study aims to review our current practice and assess the potential role of SUVmax to differentiate physiological from pathological uptake in the pituitary gland.

**Design:** A retrospective single-centre cohort study was conducted at a UK tertiary hospital.

**Patients:** Among 15824 PET-CT scans between 01/01/2017–30/06/2024, 70 patients (mean age 72.1 ± 1.3 years, 25.7% female) were included.

**Measurements:** Demographics, primary pathology, oncological treatment, SUVmax on initial PET-CT, secondary imaging findings, endocrine referral, and pituitary biochemistry were collected.

**Results:** 48 patients (68.6%) underwent secondary imaging; 70.8% ($n = 34$) were normal. Pathological findings included macroadenomas ($n = 6$), microadenomas ($n = 3$), and other lesions ($n = 5$). Mean SUVmax was significantly higher in patients with pituitary pathology (pituitary adenomas- 20.62 ± 4.82; all pathology- 16.74 ± 3.80) versus normal imaging- 4.66 ± 0.26 ($p < 0.001$). A SUVmax threshold of 4.75 yielded 100% sensitivity and 53.9% specificity for detecting pituitary pathology (ROC curve; 95% CI: 69%–100%).

**Conclusions:** Our review highlights significant variation in referral patterns for secondary imaging and to the Endocrine department. We suggest potential use of SUVmax threshold to distinguish physiological from pathological pituitary FDG uptake. Further validation in larger cohorts is warranted before routine clinical application.

Trevor Tam and Thin Kyi Phyu Naing should be considered for joint first author.

## 1 | Introduction

Positron emission tomography computed tomography (PET-CT) plays an integral role to cancer staging, treatment evaluation and surveillance [1]. Fluorine-18 labelled Fluorodeoxyglucose (FDG), a glucose analogue, is a widely used tracer [2] and serves as a surrogate marker of cellular activity. Most malignancies demonstrate increased FDG uptake compared with normal tissues, enabling earlier cancer detection than on cross-sectional imaging [3]. However, FDG is not cancer-specific, with other processes such as benign tumours, inflammation, iatrogenic causes, radiotherapy, chemotherapy and immunotherapy also demonstrating increased avidity [4, 5], leading to challenges in discriminating between benign or malignant processes or tissues. The low-dose CT component aids anatomical localisation and lesion characterisation [6]. Familiarity with benign and physiological increased FDG uptake is essential for accurate interpretation and avoiding unnecessary investigations.

PET-CT scan data undergo post-processing using reconstruction algorithms that calculate maximum Standardised Uptake Value (SUVmax), which signifies the relative ratio of uptake between two regions, forming a semiquantitative measurement of FDG uptake. SUVmax greater than mediastinal blood pool has been shown to be the most sensitive cut-off for pathological uptake in cancers such as lymphoma and non-small cell lung cancer [7].

SUVmax accuracy is influenced by factors such as injected activity, scan timing, patient weight, equipment calibration, injection-to-scan time, motion artefacts, and blood glucose levels [8, 9]. Lesion SUVmax uptake can vary by up to 20% on repeat scans in the same patient, with even greater variability across scanners [10], underscoring the need for strict control measures to ensure reproducibility.

Among various reconstruction algorithms, Vue pont HD (VPHD), once standard [11], has largely been replaced by Q clear to calculate SUVmax, which offers higher signal-to-noise ratio and therefore improving image quality [12]. Furthermore, Q clear has been shown to produce higher SUVmax when compared to conventional VPHD, allowing improved detection of sub-centimetre lesions and abnormal uptake [13].

Diagnostic SUV thresholds have been proposed for other pathologies such as pulmonary lesions [14], staging in lung cancer [7, 8, 15], adrenal lesions [16], musculoskeletal lesions [17] and gliomas [18], as well as assessing treatment response in lymphomas [19].

Rising PET-CT use in our centre has led to an increasing number of referrals for incidental pituitary FDG uptake to the Endocrine department. However, referral pathways have been inconsistent, with variability in whether secondary imaging or endocrine referral is arranged. This has led to uncertainty in clinical decision making and contributed to increased clinical burden across our radiology and endocrinology services.

At present, no UK guidelines exist for evaluating incidental pituitary FDG uptake on PET-CT scans. Our retrospective study aims to review the referral practices and secondary imaging outcomes and also explores if an SUVmax threshold can help differentiate between physiological versus pathological uptake in the pituitary gland.

## 2 | Methods

### 2.1 | Study Design

A single-centre, retrospective study of PET-CT scans was conducted to evaluate local referral patterns and secondary imaging for incidental pituitary uptake, given the absence of consistent pathways. Secondary aims were to assess whether SUVmax could serve as a discriminatory marker between physiological and pathological uptake, and to explore whether a threshold value can be proposed to aid decision making.

Our methods and results were reported according to the STROBE guidelines [20].

### 2.2 | Setting

Clinical reports of PET-CT studies containing “pituitary”, performed between the 1st of January 2017 and 30th of June 2024 at the Norfolk and Norwich University Hospital (NNUH) PET-CT scanner centre, were selected for this study. All patients with increased avidity in the pituitary gland on the PET-CT scan were included in the study.

### 2.3 | Data Collection

Data were retrospectively collected on the following fields: age, sex, primary pathology, presence of oncological treatment (i.e. chemotherapy, immunomodulatory inhibitors (immunotherapy or checkpoint inhibitor), radiotherapy or a combination of two or more of these therapies), any episode of such oncological treatment within 12 weeks preceding the PET-CT scan, SUVmax of the pituitary gland, type of secondary imaging, outcome of secondary imaging, pituitary hormone profile and outcomes of an endocrine referral, if one was made.

### 2.4 | PET-CT Scan Protocol

The PET-CT scan was performed using standard institutional protocols. From 1st January 2017 to 20th November 2019, studies were obtained using a GE 710 Discovery PET-CT mobile scanner. From 21st November 2019 onwards, studies were obtained using a GE Discovery MI DR scanner. All images were generated using the Qclear reconstruction algorithm.

All patients avoided strenuous activity for 24 h before scanning. Patients without diabetes fasted for 6 h beforehand. Patients with type 2 diabetes fasted and withheld their medication for 6 h beforehand, while type 1 diabetic patients underwent imaging at midday after a light breakfast and usual insulin, followed by a 4-h fast. Blood glucose concentration was measured before injection; those with concentrations of $< 12$ mmol/l received the 18F-fluorodeoxyglucose (18-FDG) injection, whilst those

> 12 mmol/l were rebooked. The dose was calculated according to the patient's weight. Following injection, patients rested for 1 h before scanning. The tracer dose (megabecquerel), half-life (seconds) and injection-to-scan time were recorded for each patient. PET-CT images were interpreted by seven different consultant radiologists with special interest in Nuclear Medicine.

### 2.5 | Statistical Analysis

Statistics were performed using the IBM SPSS Statistics Software Version 29.0.2.0. Descriptive statistics, including mean and standard deviation, were used to summarise patient demographics, primary malignancy types, imaging outcomes and SUVmax values. Continuous variables are expressed as mean ± standard deviation of the mean (SEM) or median and interquartile range (IQR), as appropriate. An independent (unpaired) samples t-test compared mean SUVmax of patients with pituitary adenomas, pathology on secondary imaging, and those with normal imaging. Statistical significance was defined as a $p$-value < 0.05.

Receiver operating characteristic (ROC) curve analysis with logistic regression was used to establish an optimal SUVmax threshold for differentiating physiological from pathological uptake in the pituitary gland. Sensitivity and specificity were calculated, with the threshold SUVmax selected to maximise sensitivity for screening purposes while maintaining an acceptable level of specificity. A Spearman's rank correlation was used to assess tumour size correlation with SUVmax.

### 2.6 | Ethics

Ethics approval was deemed not required by the Medical Research Council's NHS Research Ethics Committee Tool.

## 3 | Results

### 3.1 | Patient and Sample Characteristics

Over a 7.5-year period (1/1/2017–30/6/2024), our centre had a total of 15824 PET-CT scans. Out of the 15824 scans, 70/15824 (0.44%) patients were included after applying exclusion criteria (Figure 1). Of the 70 patients, 18/70 (25.7%) patients were female. The mean (± SD) age of patients was 72.1 ± 1.3 years old.

5/70 (7.1%) patients were scanned with the GE 710 Discovery PET-CT mobile scanner before 21/11/2019. 65/70 (92.9%) patients were scanned with the GE Discovery MI DR scanner.

### 3.2 | Primary Pathology

In the 70 patients, 27/70 (38.6%) of primary malignancies were of haematological origin, followed by 19/70 (27.1%) being dermatological, 9/70 (12.9%) being respiratory, 4/70 (5.7%) being otorhinolaryngological, 1/70 (1.4%) being urological, 1/70 (1.4%) being endocrine, and 1/70 (1.4%) being thymic.

8/70 (11.4%) of patients had nonmalignant primary disease, which included IgA and IgM Kappa Paraproteins, polymyalgia rheumatica, primary sclerosing cholangitis, ulceration of the cervical oesophagus, pyrexia of unknown origin, large vessel vasculitis, and two with monoclonal gammopathy of unknown significance (Table 1).

### 3.3 | Oncological Treatments

A total of 36/70 (51.4%) patients had received oncological treatments. Out of the 36 patients, 21/36 (58.3%) received immunomodulatory inhibitors (including immunotherapy (7/21, 33.3%) and checkpoint inhibitors (14/21, 66.7%); 8/36 (22.2%) received chemotherapy, and 3/36 (8.3%) received radiotherapy, while 4/36 (11.1%) received combination therapy (1/4 (25%) immunotherapy + radiotherapy; 2/4 (50%) chemotherapy + radiotherapy; 1/4 25%) immunotherapy + chemotherapy). 27/36 (75%) had received treatment within 12 weeks before PET-CT scan.

The remaining 34/70 (48.5%) patients did not receive these treatments.

### 3.4 | Referral Patterns and Secondary Imaging

Out of the 70 patients, 48/70 (68.6%) of patients received secondary imaging. Out of the 48 patients, 23/48 (33.8%) were MRI Pituitary scans, 21/48 (30.9%) were CT Head scans, and 3/48 (4.4%) were MRI Head scans. 1/48 (1.47%) underwent a CT Pituitary scan. 22/70 (31.4%) had no further imaging.

Of the 48 patients with secondary imaging, 34/70 (70.8%) were found to be normal.

Of the remaining 14/48 (29.2%) patients, 9/14 (64.3%) were found to have pituitary micro or macroadenomas. This included 6/14 (42.9%) with macroadenomas and 3/14 (21.4%) with microadenomas.

Of the remaining 5/14 (35.7%), 2/14 (14/3%) were found to have metastatic spread of their primary malignancy (non-small cell lung cancer and CNS lymphoma respectively), 1/14 (7.1%) was found to have nonspecific pituitary enlargement, 1/14 (7.1%) had radiological evidence of osmotic demyelination syndrome, and 1/14 (7.1%) had dual pathology i.e., pituitary microadenoma and metastatic disease.

Of the 8/70 (11.4%) patients who had nonmalignant primary disease, 3/8 (37.5%) were found to have pathology on secondary imaging. Patient ID 4 was found to have a 13 mm nonspecific pituitary enlargement but was deceased before referral to Endocrine. ID 5 was found to have 20 mm osmotic demyelination syndrome and was not referred to Endocrine, whilst ID 7 was found to have a 4 mm microadenoma and was referred to Endocrine (Table 1).

Of the 14/70 (20%) patients demonstrating abnormal pituitary appearances, 11/14 (78.6%) underwent pituitary hormone blood

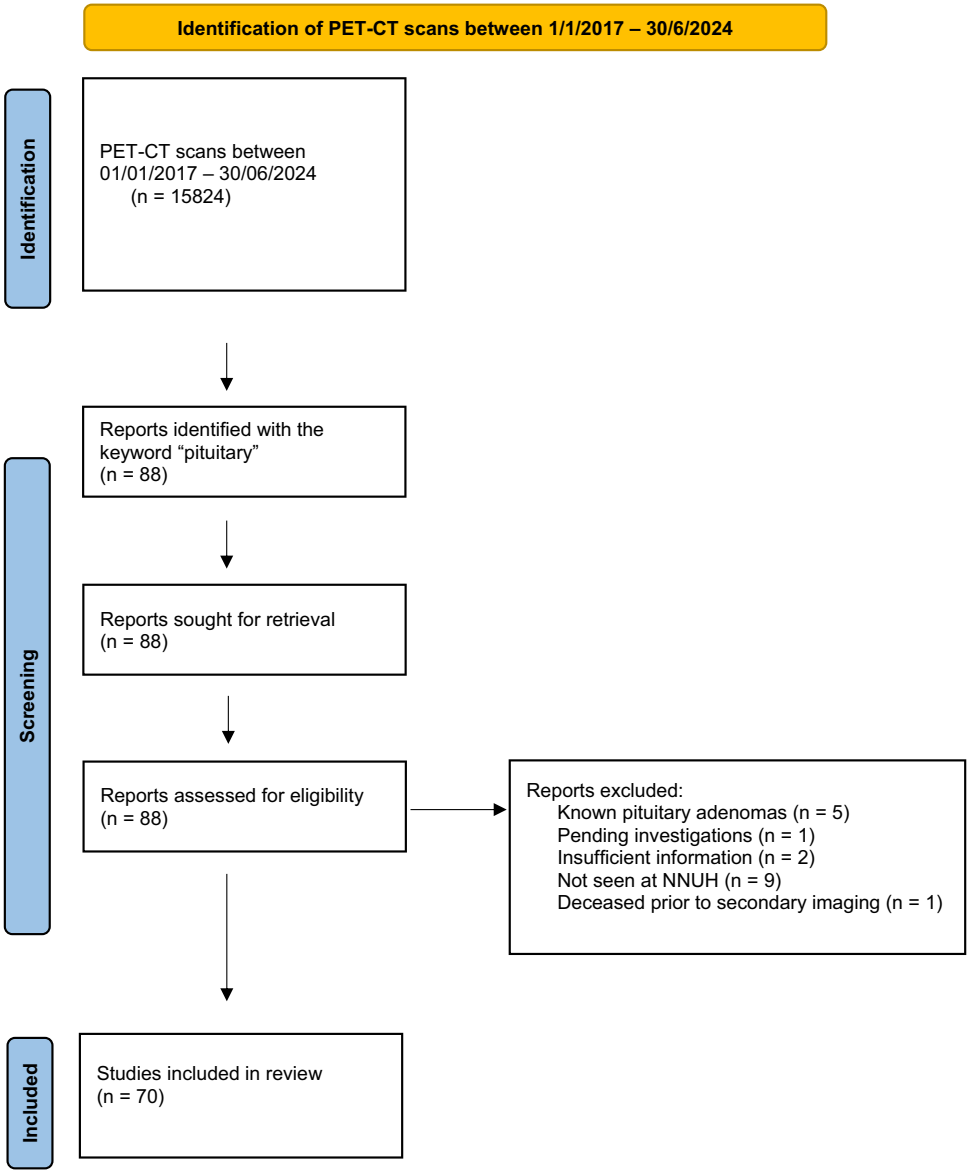


**FIGURE 1** | Flowchart of patient selection for final data analysis.

testing. Of these 11, 9/11 (81.8%) were eupituitary, 1/11 (9.1%) had raised prolactin, and the remaining 1/11 (9.1%) had partial hypopituitarism (low thyroid-stimulating hormone) (Table 2).

### 3.5 | Referral to the Endocrinology Department

Out of the 70 patients, 18/70 (25.7%) were referred to the Endocrine while 52/70 (74.3%) were not.

Of the 18/70 (25.7%) patients who were referred to Endocrine, all received secondary imaging. 7/18 (38.9%) were discharged after having normal secondary imaging. The remaining 11/18 (61.1%) patients demonstrated abnormal pituitary appearance.

Out of these 11 patients, 9/11 (81.2%) were found to have pituitary micro or macroadenomas, 1/11 (9.1%) had a metastatic spread of their primary malignancy, and the remaining 1/11 (9.1%) was found to have dual pathology (microadenoma + metastatic disease).

All 11 patients were managed either medically (1/11 (9.1%), cabergoline for macroprolactinoma) or conservatively (10/11, 90.9%) from an endocrine perspective.

Table 2 summarises the baseline characteristics of patients who had positive secondary imaging.

### 3.6 | SUVmax Uptake Values

7.1% ($n = 5$) patients were scanned with the GE 710 Discovery PET-CT mobile scanner before 21/11/2019. 92.9% ($n = 65$) patients were scanned with the GE Discovery MI DR scanner, with no statistically significant difference in SUVmax values between the scanners ($p = 0.758$) (Mann Whitney $U$ test).

**SUVmax of all positive secondary imaging:** (pituitary adenoma + other pathologies, including malignancy) (Table 2)

**TABLE 1** | Baseline characteristics of patients who had nonmalignant primary disease with incidental FDG uptake in the Pituitary Gland.

| ID | Age | Gender | Primary pathology | SUVmax (Qclear) | Type of secondary imaging | Outcome of secondary imaging | Referral to Endocrinology |
|---|---|---|---|---|---|---|---|
| 1 | 86 | F | IgA Kappa + IgM Kappa Paraproteins | 3.0 | MRI Pituitary | Normal | Not referred |
| 2 | 72 | M | Polymyalgia rheumatica | 3.3 | No scan | Scan not done | Not referred |
| 3 | 81 | M | Primary sclerosing cholangitis | 26.7 | No scan | Scan not done | Not referred |
| 4 | 86 | M | Ulceration of the cervical oesophagus | 7.8 | MRI Pituitary | 13 mm nonspecific pituitary enlargement | Not referred |
| 5 | 70 | M | Pyrexia of unknown origin | 4.9 | MRI Pituitary | 20 mm osmotic demyelination syndrome | Not referred |
| 6 | 69 | M | Large vessel vasculitis | 3.4 | No scan | Scan not done | Not referred |
| 7 | 76 | M | Monoclonal gammopathy of undetermined significance | 19.3 | MRI Pituitary | 4 mm microadenoma | Referred |
| 8 | 84 | M | Monoclonal gammopathy of undetermined significance | 4.2 | MRI Pituitary | Normal | Not referred |

The mean SUVmax uptake in all patients (mean age $76.1 \pm 2.4$ years old, 100% males) with positive secondary imaging (pituitary adenoma + other pathologies including malignancy) was $16.74 \pm 3.80$ (range 4.8–57.2).

### 3.7 | SUVmax of All Positive Secondary Imaging Vs Normal Imaging

There was a statistically significant difference ($p < 0.001$) between the mean uptake in patients with positive secondary imaging (pituitary adenoma + other pathologies, including malignancy), when compared to the mean uptake in patients with normal secondary imaging. The mean SUVmax difference was $12.08 \pm 2.43$ (95% CI: 7.18–16.98) higher in the positive secondary imaging group than the normal imaging group.

### 3.8 | SUVmax of Pituitary Adenomas on Secondary Imaging

The mean SUVmax uptake amongst patients (mean age $76.6 \pm 3.0$ years old, 100% males) found to have a pituitary adenoma was $20.62 \pm 4.82$ (range 4.8–57.2).

There was also a statistically significant, strong positive correlation between SUVmax value and pituitary tumour size (Spearman's rank correlation: 0.817, $p = 0.007$) (Figure 2).

### 3.9 | SUVmax of Pituitary Adenomas Vs Normal Imaging

There was a statistically significant difference ($p < 0.001$) between the mean uptake in patients with incidentally found pituitary lesions on secondary imaging, when compared to the mean uptake in patients with normal secondary imaging. The mean SUVmax difference was $15.96 \pm 2.58$ (95% CI: 10.75–21.18) higher in the pituitary adenoma group than the normal imaging group.

### 3.10 | Normal Secondary Imaging

The mean SUVmax uptake in patients (mean age $69.2 \pm 1.9$ years old, 64.7% (22/34) males) who had normal pituitary appearances on secondary imaging was $4.66 \pm 0.26$ (range 2.9–9.1).

### 3.11 | Patients Who Did Not Receive Secondary Imaging

The median SUVmax uptake in patients who did not receive secondary imaging was 5.65 (IQR 4.13–6.7, range 3.3–26.7).

### 3.12 | SUVmax of Positive Secondary Imaging Vs No Secondary Imaging

There was a statistically significant difference ($p < 0.001$) between the mean uptake in patients with positive secondary imaging (pituitary adenoma + other pathologies, including malignancy), when compared to the mean uptake in patients who did not receive secondary imaging.

### 3.13 | SUVmax of No Secondary Imaging Vs Normal Imaging

There was no statistically significant difference ($p = 1.000$) between the mean uptake in patients who did not receive secondary imaging and those who had normal secondary imaging.

Results are summarised in Table 3.

**TABLE 2** | Baseline characteristics of patients who had positive secondary imaging.

| Age | Gender | SUVmax (Qclear) | Outcome of secondary imaging | Type of secondary imaging | Type of primary malignancy or pathology | Details of primary malignancy or pathology | Functional status of pituitary lesion | Type of oncological treatment | Oncological treatments within previous 12 weeks | Referral to Endocrinology |
|---|---|---|---|---|---|---|---|---|---|---|
| 81 | M | 57.2 | 13 mm macroadenoma | MRI Pituitary | Haematological | Multiple myeloma | Eupituitary | No treatment | N/A | Referred |
| 71 | M | 14.3 | 10 mm macroadenoma | MRI Pituitary | Haematological | Lymphoma | Eupituitary | No treatment | N/A | Referred |
| 88 | M | 13.2 | 10 mm macroadenoma | MRI Pituitary | Haematological | Lymphoma | Eupituitary | No treatment | N/A | Referred |
| 89 | M | 14.0 | 9 mm microadenoma | MRI Pituitary | Haematological | Lymphoma | Eupituitary | No treatment | N/A | Referred |
| 81 | M | 4.8 | Dual pathology (2.5 mm microadenoma + 16 mm bony metastasis in clivus) | MRI Pituitary | Urological | Malignant neoplasm of prostate | Eupituitary | No treatment | N/A | Referred |
| 69 | M | 6.3 | CNS lymphoma (involving distal thoracic spinal cord, cauda equina and multiple exiting nerves in the lumbar spine in keeping with Stage 1E) (unable to measure) | CT Head | Haematological | Lymphoma | Biochemistry not done | Immunomodulatory inhibitor (checkpoint inhibitor) | No | Not referred |
| 75 | M | 9.2 | 9 mm metastatic hypothalamic nodule- anterior to the pituitary stalk - diagnosed as pituitary metastasis following multidisciplinary team meeting | MRI Head | Respiratory | Non-small cell lung cancer | Partial hypopituitarism (low thyroid stimulating hormone) | No treatment | N/A | Referred |

(Continues)

**TABLE 2** | (Continued)

| Age | Gender | SUVmax (Qclear) | Outcome of secondary imaging | Type of secondary imaging | Type of primary malignancy or pathology | Details of primary malignancy or pathology | Functional status of pituitary lesion | Type of oncological treatment | Oncological treatments within previous 12 weeks | Referral to Endocrinology |
|---|---|---|---|---|---|---|---|---|---|---|
| 86 | M | 7.8 | 13 mm nonspecific pituitary enlargement | MRI Pituitary | Nonmalignant disease | Ulceration in cervical oesophagus | Biochemistry not done | N/A | N/A | Not referred |
| 70 | M | 4.9 | 20 mm osmotic demyelination syndrome | MRI Pituitary | Nonmalignant disease | Pyrexia of unknown origin | Biochemistry not done | N/A | N/A | Not referred |
| 70 | M | 21.6 | 10 mm macroadenoma | MRI Pituitary | Haematological | Lymphoma | Eupituitary | Chemotherapy | Yes | Referred |
| 76 | M | 19.3 | 4 mm microadenoma | MRI pituitary | Nonmalignant disease | Monoclonal gammopathy of undetermined significance | Eupituitary | Immunomodulatory inhibitor (immunotherapy) | Yes | Referred |
| 72 | M | 10.8 | 9 mm microadenoma | MRI pituitary | Dermatological | Melanoma | Eupituitary | No treatment | N/A | Referred |
| 57 | M | 15.1 | 29 mm macroadenoma (Prolactinoma) | MRI pituitary | Respiratory | Lung cancer | Raised prolactin[a] (86,326) | Chemotherapy | Yes | Referred |
| 81 | M | 35.9 | 12 mm macroadenoma | MRI pituitary | Respiratory | Lung cancer | Eupituitary | No treatment | N/A | Referred |

[a]Units: 86,326 mIU/L, reference range: 40–530 (4057.32 ng/mL, reference range: 1.88–24.91).
[a]MALT, mucosa-associated lymphoid tissue; MGUS, monoclonal gammopathy of undetermined significance; N/A, not applicable; CNS, central nervous system.

## 4 | Discussion

### 4.1 | Principal Findings

The incidence of detecting increased pituitary uptake on PET-CT in our cohort was low at 0.44%. Our retrospective study also highlights significant variation in referral patterns for secondary imaging (48/70, 68.6%) and to the Endocrine department (18/70, 25.7%). Reassuringly, in those who had secondary scans, the majority (34/48, 70.8%) had normal pituitary appearances.

Our study has also shown that patients with incidentally found pituitary adenomas ($20.62 \pm 4.82$) and those with positive secondary imaging (pituitary adenomas + other pathologies) ($16.74 \pm 3.8$) had significantly higher SUVmax values than those with normal imaging ($4.66 \pm 0.26$) ($p < 0.001$).

Notably, amongst patients who did not undergo secondary imaging, the median SUVmax value was not found to be statistically different ($p = 1.000$) from those who had normal secondary imaging.

Given the absence of standardised guidance, our work serves as a review of our local practice, highlighting variation in referral patterns, and proposes the potential for SUVmax to be integrated into future diagnostic algorithms.

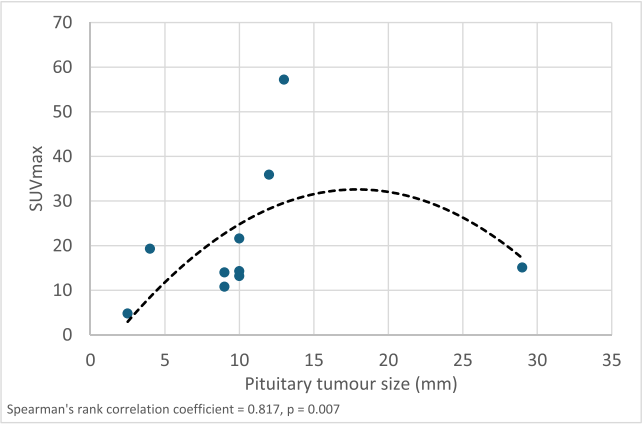


**FIGURE 2** | Correlation between pituitary tumour size and SUVmax.

### 4.2 | Comparison with Related Literature

#### 4.2.1 | Clinical Significance and Incidence of Pituitary Adenomas

Pituitary uptake on PET-CT may be physiological or pathological due to benign (functioning or nonfunctioning) or malignant tumours. Regardless of the aetiology, large pituitary tumours may cause complications such as visual field defects, hypopituitarism, and arginine vasopressin deficiency from mass effect, and require lifelong follow-up due to their growth potential [21]. Thus, accurate characterisation is essential to guide treatment and avoid missed diagnoses.

Owing to its rarity, the incidence of pituitary adenomas on PET-CT scan is not widely discussed in literature, and no guidelines currently exist in the UK for their assessment and management. Despite this, incidental pituitary uptake on PET-CT is most often due to an adenoma [22–25], with a smaller percentage due to metastases or other pituitary lesions [22].

Reported incidence of incidental pituitary uptake on PET-CT scans was 0.33% [26] and 0.22% [25] respectively, comparable to our 0.44%. A multicentre review of 40967 patients found 0.073% incidence and mean SUVmax of $8.9 \pm 6.6$ (range: 3.2–32.6), compared with our $16.74 \pm 3.8$ (range: 4.8–57.2), though no SUVmax threshold was proposed [23].

By comparison, incidental pituitary lesions detected on MRI had a pooled prevalence of 0.27% [27], lower than our incidence of 0.44%. Pituitary uptake by other radiotracers such as $^{68}$Ga-DOTATATE, $^{68}$Ga-DOTATOC and $^{18}$F-choline has also been reported [28, 29].

#### 4.2.2 | Role of SUvmax in Determining Physiological Vs Pathological Uptake

Of the 70 patients in our study, 68.6% ($n = 48$) underwent secondary imaging, with 29.2% ($n = 14$) demonstrating pathology-most commonly pituitary macroadenomas ($n = 6$) and microadenomas ($n = 3$), consistent with previous evidence [22–25]. Other findings included metastasis ($n = 2$), nonspecific pituitary

**TABLE 3** | SUVmax values of patients with incidental pituitary uptake, stratified according to secondary imaging outcome.

| Group | Number of patients | Mean/median SUVmax | SUVmax range | Comparison with normal secondary imaging |
|---|---|---|---|---|
| Normal secondary imaging | 34 | Mean: $4.66 \pm$[a] 0.26 | 2.9–9.1 | — |
| All positive secondary imaging (pituitary adenomas + other pathology) | 14 | Mean: $16.74 \pm 3.80$ | 4.8–57.2 | $12.08 \pm 2.43$ (95% CI: 7.18–16.98) higher than normal secondary imaging ($p < 0.001$) |
| Pituitary adenoma on secondary imaging | 9 | Mean: $20.62 \pm 4.82$ | 4.8–57.2 | $15.96 \pm 2.58$ (95% CI: 10.75–21.18) higher than normal secondary imaging ($p < 0.001$) |
| No secondary imaging | 22 | Median: 5.65 (IQR 4.13–6.7) | 3.3–26.7 | No statistically significant difference from normal secondary imaging ($p = 1.000$) |

[a]Values are presented as mean ± standard deviation of the mean (SEM) unless otherwise stated.

enlargement ($n = 1$), osmotic demyelination syndrome ($n = 1$), and dual pathology (microadenoma + metastatic disease) ($n = 1$).

Patients with pathology on secondary imaging had significantly higher SUVmax than those with normal imaging ($p < 0.001$), suggesting SUVmax can be effective in distinguishing physiological from pathological uptake in the pituitary gland, and no difference was observed between patients with or without a primary malignancy. SUVmax correlated with lesion size ($p = 0.018$), consistent with prior studies [1, 23, 24].

Mean SUVmax of patients with pituitary adenoma on secondary imaging was $20.62 \pm 4.82$, (range 4.8–57.2), and was statistically significantly higher than normal imaging ($4.66 \pm 0.26$, $p < 0.001$). Notably, our value is higher than previous means of $10.31 \pm 7.85$ [25], $11.5 \pm 8.4$ [23], and $10.9 \pm 7.0$ [30], respectively.

SUVmax was unaffected by recent oncological treatment (within 12 weeks before the scan), despite concerns about erroneous inflammatory uptake [6] and hypophysitis post-immunotherapy [31]. Immunotherapy-induced hypopituitarism occurred in one patient but overall, treatment did not alter SUVmax.

These findings suggest that SUVmax may be a potential discriminator of benign and pathological uptake in a heterogeneous patient population, independent of patient demographics, primary pathology, or treatment. Previous studies support PET-CT in detecting pituitary functional changes [32], especially when combined with MRI [33]. In particular, the Qclear can further improve accuracy of reconstructed spatial resolutions [12], as demonstrated in other pathologies such as breast cancers [13] and lymphomas [11].

#### 4.2.3 | Proposed SUVmax Thresholds in the Literature

A threshold value of 4.1 has been suggested [30], which reportedly is 96.6% sensitive and 88.1% specific for pituitary pathology. However, an alternative threshold of 2.4 from a prospective study has also been suggested [1], which reportedly has a 94.7% sensitivity and 100% specificity for pituitary microadenomas, suggesting that the 4.1 threshold value may potentially miss small lesions.

SUVmax has also proven useful with other tracers such as $^{11}$C-methionine and $^{13}$N-ammonia, demonstrating higher uptake in adenomas compared with normal imaging ($3.29 \pm 0.76$ vs $2.14 \pm 1.29$, $2.28 \pm 0.60$ vs $1.30 \pm 1.05$), respectively [34].

#### 4.2.4 | Role of SUVmax Thresholds In Other Pathologies

Diagnostic SUVmax thresholds have been proposed for other pathologies such as pulmonary lesions [6], lung cancer [7, 8, 15], adrenal lesions [16], musculoskeletal lesions [17] and gliomas [18], as well as assessing treatment response in lymphomas [19]. However, currently there are no UK guidelines for evaluating incidental pituitary FDG uptake on PET-CT scans.

### 4.3 | Strengths and Limitations

Our study has several strengths. The statistically significant difference in SUVmax between pituitary adenomas and normal imaging on secondary scans supports its role as a diagnostic marker, providing an objective and quantifiable metric for clinical decision-making. The strong correlation identified between SUVmax and tumour size ($\rho = 0.817$, $p = 0.007$) further highlights its clinical value. Additionally, our proposal of an SUVmax threshold to differentiate physiological from pathological pituitary uptake can help standardise PET-CT interpretation of incidental pituitary findings. Use of secondary imaging validates these findings and helps refine diagnostic pathways.

We acknowledge the limitations in our study. The single-centre, retrospective design and small sample size of our study, albeit reaching statistical significance, require confirmation with larger studies. Owing to the retrospective nature of the study, there was missing data, such as secondary imaging and biochemistry values, and the lack of histological confirmation, which may have affected results. Patients were also scanned using two different PET-CT scanners: five patients were imaged using the older GE 710 Discovery PET-CT mobile scanner, while 65 patients were scanned using the newer GE Discovery MI DR scanner. Despite this, there was no statistically significant difference in SUVmax values between the two scanner groups ($p = 0.758$), suggesting that scanner variability did not impact the consistency of SUVmax measurements in our analysis. Another limitation is that patient identification relied on radiology reports rather than systematic image re-review. While this reflects real-world referral practice, it may underestimate the true incidence of pituitary FDG uptake. Future studies incorporating an independent image review can help quantify overlooked cases and improve detection accuracy.

Despite these limitations, the findings are promising, and serves as a valuable foundation for larger, prospective, multicentre studies where imaging, radiological, and histological data are investigated, to validate the conclusions drawn from this study.

### 4.4 | Proposed Pathway for the Investigation and Management of Incidentally Found Pituitary Adenomas

The incidence of pituitary adenomas on PET-CT is low, but it is likely to rise given the increasing use of imaging, growing rates of malignancy along with an aging patient population.

In line with Pituitary Society international guidelines [35], we recommend an MRI pituitary as 1st line following positive FDG uptake as it provides a high-resolution image focused on the pituitary. A CT scan of the Pituitary can be considered for patients with MRI contraindications. Should the secondary imaging be positive, patients should then be referred to Endocrinology for a biochemical and clinical assessment to determine lesion functionality, symptoms, to decide on further management and follow-up (Figure 3).

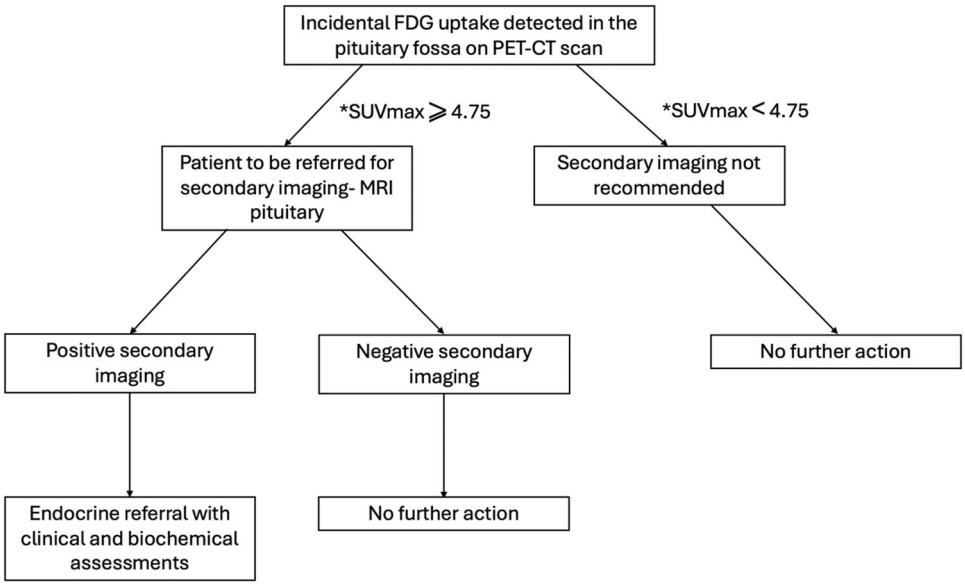


**FIGURE 3** | Proposed pathway for the investigation and management of incidentally found pituitary adenomas detected on PET-CT scans. *The 4.75 threshold is based on our limited dataset. Further power calculations and more data are needed to investigate these findings.

Therefore, we propose that, to minimise unwarranted referrals and reduce healthcare-associated burden, in patients with incidental pituitary FDG uptake, secondary imaging should be arranged **before referral to Endocrinology**.

## 5 | Conclusion and Recommendations

Our retrospective study shows that in 15824 PET-CT scans performed between 1/1/2017–30/6/2024, 70 (0.44%) were found to have incidental pituitary FDG uptake. Of these, 48/70 (68.6%) received secondary imaging, with 14/48 (29.1%) demonstrating positive secondary imaging.

In our limited cohort, patients with incidentally found pituitary adenomas have a significantly higher SUVmax value ($20.62 \pm 4.82$) compared to those with normal imaging ($4.66 \pm 0.26$) ($p < 0.001$). This potentially suggests a role for SUVmax value as a discriminator between physiological and pathological FDG uptake within the pituitary fossa. Our study also alludes to, albeit from a small dataset, an SUVmax value of 4.75 as a threshold (100% sensitive and 53.9% specific, 95% CI: 69%–100%), to differentiate between physiological versus pathological uptake in the pituitary gland.

However, appropriately powered, case-controlled studies are warranted to further investigate this value.

### Author Contributions

Conceptualisation, R.A; Data curation, T.T. and T.K.P.N.; Formal analysis, T.T., Investigation, T.T., T.K.P.N., L.B., R.R.B.; Methodology, Rupa Ahluwalia; Supervision, R.A; Validation, R.R.B., Visualisation, T.T. and T.K.P.N.; Writing- original draft, T.T. and T.K.P.N.; Writing- review and editing, F.S., K.D. and Rupa Ahluwalia. All authors have read and agreed to the published version of the manuscript.

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### Conflicts of Interest

The authors declare no conflicts of interest.

### Data Availability Statement

The authors confirm that the data supporting the findings of this study are available within the article.

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