

## **Characteristics of pituitary adenomas detected on FDG-PET/CT for cancer screening**

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## **Abstract**

The Southern Tohoku Healthcare Group has been using PET/CT (computed tomography) for early detection of cancer since the early days of its application. We have unexpectedly found the rate detecting asymptomatic pituitary adenomas to be rather high, approaching 3%, in the population receiving health check-ups using PET at our hospital. Pituitary adenomas have been detected and treated in 17 patients. In order to identify the characteristics of these 17 patients, we examined the following variables: the maximum standardized uptake value (SUVmax) on PET, histopathological classification, growth potential, hormone production, and tumor volume. There was a significant positive correlation between the SUVmax and growth potential. Pituitary adenomas detected on FDG-PET/CT cancer screening require prompt treatment because these tumors are associated with relatively high growth potential.

## **Introduction**

The cancer detection rate in the population undergoing health check-ups using PET (positron emission tomography) in Japan was reported to be approximately 2%. The Southern Tohoku Healthcare Group has been using PET/CT (computed tomography) for early detection of cancer since the early days of its application. The cancer detection rate with the screening program at our hospital has reached 2.7%, slightly higher than the national average. We have unexpectedly found the rate detecting asymptomatic pituitary adenomas to be rather high, approaching 3%, in the population receiving health check-ups using PET at our hospital. This rate is markedly higher than that reported in a previous study.<sup>1)</sup> Herein, we sought to determine the characteristics of pituitary adenomas detected during health check-ups using FDG (fluorodeoxyglucose)-PET.

## **Objectives**

PET was introduced at our hospital in 2004 and has been used for cancer-related health check-ups since 2005. The detection rate of pituitary adenoma has increased since 2008. To date, pituitary adenomas have been detected and treated in 17 patients. In order to identify the characteristics of these 17 patients, we examined the following variables: the maximum standardized uptake value (SUVmax) on PET, histopathological classification, growth potential, hormone production, and tumor volume.

## **Subjects**

The 17 subjects of this study had pituitary disorders detected on health check-ups using FDG-PET and subsequently treated during a period of about 5 years between January 2008 and November 2012. The total number of participants in the health check-up program using PET during the study period was 628, such that the 17 subjects accounted for approximately 3% of the total. The detection rate for other cancers during this period totaled 2.7%. In addition, the number of patients who underwent pituitary surgery at our hospital during the period was 560, with the 17 subjects accounting for 2% of the total. Our 17 subjects consisted of 12 men and 5 women, with a mean age of 65, range 50 to 76, years. The histopathological diagnoses included 9 plurihormonal adenomas, 4 gonadotroph cell adenomas, 1 preclinical Cushing's disease, and 3 others. The average tumor volume was 870 mm<sup>3</sup>, range 4 to 4400 mm<sup>3</sup>. Although none of the subjects had symptoms at the time of the health check-up, 4 of the 17 complained of symptoms such as headache, dizziness, and visual field defect when they were subsequently examined by specialists at the outpatient clinic. In addition, 1 patient was diagnosed with preclinical Cushing's disease based on endocrine test results.

## **Methods**

### ***Neuroimaging***

Examinations using PET are an option offered as part of our complete health check-up program. We refer to this as PET cancer screening. During the PET procedure, 5mL of FDG are injected into the subject, and the blood glucose level is measured and then corrected for analysis. The instruments used for the study are PET/CT (Discovery LS, GE Medical Systems), PET (Advance NX/I, GE Medical Systems), and multi-detector CTs (Light Speed Ultra 16 and Light Speed Plus beta, GE Medical Systems). The SUV is defined as the radioactivity concentration of the region of interest divided by the relative injected radioactivity. The subjects underwent whole-body scanning. Delayed scanning of FDG, at 60 and 120 minutes after injection, was performed because FDG uptake is delayed in some types of cancer. Figure shows a FDG-PET image obtained at our hospital. The PET image was fused with the corresponding CT scan, and the SUVmax in the region of interest was calculated. Those subjects who showed abnormal uptake in the region of interest were referred to the brain surgery outpatient clinic for further examination. Statistical analysis of differences was performed using the Student *t* test. Correlations of the SUVmax with histopathological classification, growth potential, hormone production, and tumor size were analyzed.

### ***Pathological investigation***

Surgical specimens were fixed in 10% neutral buffered formalin and embedded in paraffin. 3 mm thick slices were prepared and stained with hematoxylin and eosin. Immunohistochemical staining was performed by the ABC method using the following antibodies; polyclonal adrenocorticotrophic hormone (DAKO, Tokyo, Japan), polyclonal growth hormone (DAKO, Tokyo, Japan), polyclonal prolactin (DAKO, Tokyo, Japan), monoclonal thyroid-stimulating hormone-beta (Neo markers, CA, USA), monoclonal luteinizing hormone-beta (Neo markers, CA, USA),

monoclonal follicle-stimulating hormone-beta (Neo markers, CA, USA), polyclonal  $\alpha$ -subunit (DAKO, Tokyo, Japan) and monoclonal Ki-67 (DAKO, Tokyo, Japan).

## **Results**

The characteristics of the 17 subjects are shown in Table 1. The mean SUVmax was 13.2, markedly higher than the 3.6 obtained in previously examined pituitary adenoma patients at our hospital (Fig 1). With regard to growth potential, the mean MIB-1 index in our present subjects was substantially higher than the value of 1.2% obtained when examining conventional adenocarcinomas.<sup>2)</sup> It is noteworthy that 6 patients had adenomas with growth potential values of 4% or more. The mean number of hormones secreted was 3.8, markedly higher than the 2.8 of growth hormone-producing adenomas, which reportedly secrete a relatively large number of hormones, and the 1.2 of prolactin-producing adenomas.<sup>3)</sup>

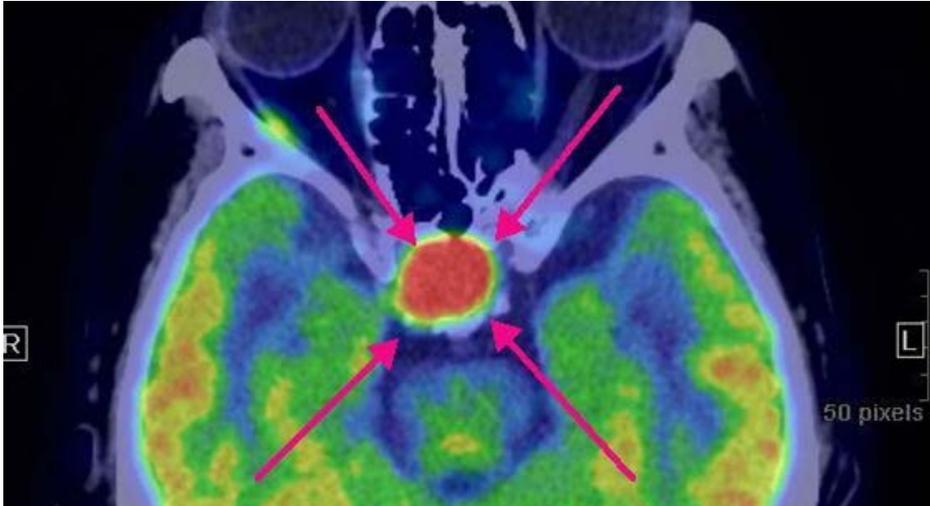
We also examined the relationships between SUVmax on PET and other variables. There was no significant correlation between SUVmax and tumor volume ( $p = 0.12$ ). Likewise, there was no significant correlation between SUVmax and histopathological classification ( $p = 0.78$ ). Although 70% of our 17 subjects had plurihormonal adenomas, there was no significant association between SUVmax and the number of hormones secreted ( $p = 0.071$ ). A statistically significant association was recognized between SUVmax and growth potential ( $p = 0.0025$ ); that is, growth potential increased as SUVmax increased.

Table 1. The clinic-pathological detail of all patients.

	Sex	Age (y)	Histopathological diagnosis	Volume (cc)	No of hormones	Ki-67 labelling index	SUV max
1	M	54	Gonadotroph	4400	1	1.2	4.8
2	M	58	Atypical plurihormonal	1890	3	2.5	19.1
3	F	63	Plurihormonal	171	5	1.5	5.9
4	F	60	Plurihormonal	150	5	2.7	6.1
5	M	66	Pre-clinical Cushing	4	5	1.5	5.9
6	F	76	Gonadotroph	28	2	2.9	6.9
7	M	66	Plurihormonal & Gonadotroph	324	5	8.8	15.3
8	M	64	Plurihormonal	480	3	14.2	24.3
9	M	70	Gonadotroph	1615	2	4.7	9.5
10	M	72	Plurihormonal (Oncocytoma)	1287	3	16.5	19.3
11	F	74	Plurihormonal	60	5	2.2	6.7
12	F	64	Gonadotroph (Oncocytoma)	1785	2	7.8	14.5
13	M	60	Plurihormonal (Polymorphous)	468	4	1.4	10.4
14	M	65	Plurihormonal	171	5	4.7	11.7
15	M	50	Plurihormonal	484	5	4.8	5.2
16	M	71	Plurihormonal	140	5	1	3.7

Figure.1 PET/CT fusion image

Red arrows indicate accumulation of FDG in the pituitary region.



## Discussion

The present results suggest pituitary adenomas detected on FDG-PET cancer screening to be associated with higher SUVmax, indicating greater growth potential. Increased glucose metabolism within adenomas suggests a high likelihood of growth and progression to malignant tumors. In addition, although many were plurihormonal, nonfunctioning adenomas, most had MIB-1 values of 3% or more, suggesting a resemblance to so-called atypical tumors. In 4 of the 17 cases, electron microscopic examination was performed: oncocytoma was diagnosed in 2, polymorphous type in 1, and atypical adenoma in 1, suggesting that some of these patients had highly invasive tumors and/or were likely to develop pituitary dysfunction.

The present results highlight the importance of early diagnosis and treatment for individuals with pituitary adenomas detected on FDG-PET/CT cancer screening.

## **Conclusions**

1. The characteristics of asymptomatic pituitary adenoma detected on FDG-PET/CT were examined by measuring the SUVmax and other variables.

2. The pituitary adenomas detected on FDG-PET/CT cancer screening were associated with higher SUVmax, indicating greater growth potential. Many were plurihormonal adenomas.

3. There was a significant positive correlation between the SUVmax and growth potential.

4. Pituitary adenomas detected on FDG-PET/CT cancer screening require prompt treatment because these tumors are associated with relatively high growth potential.

## References

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