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# FDG uptake in the morphologically normal thymus: comparison of FDG positron emission tomography and CT

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**Abstract.** The purpose of this study was to evaluate the correlation between fluorine-18 fluorodeoxyglucose (FDG) thymic uptake and a normal appearing thymus on CT. Non-attenuation corrected FDG positron emission tomography (PET) data from 94 young persons (mean age 25.4 years, range 18–29 years) with a normal thymus diagnosed on CT were retrospectively evaluated. No subject had clinical symptoms suggestive of thymus-related disease or mediastinal tumour (follow-up period 6–69 months). PET images were visually assessed and the count ratio between the thymus and the lung (T/L ratio) was calculated. Increased FDG uptake occurred in 32 (34%) subjects. In these 32 cases, the T/L ratio was $2.86 \pm 0.49$ (range 2.02–3.99). In 86 subjects whose CT images were available to calculate the CT attenuation of the thymus (CAT), the CAT value was $-17.5 \pm 45.7$ HU (range –103.6 HU to 79.9 HU). The T/L ratio correlated with the CAT value ($r=0.58$). CAT values in subjects with positive PET findings were significantly higher than CAT values in subjects with negative PET findings ($p<0.001$, unpaired *t*-test). These results suggest that even in young adults, if the thymus has a relatively high CT attenuation value, the presence of physiological thymic uptake in FDG-PET is a normal variant. In this study, the diagnosis of normal thymus was based on CT appearance and clinical course. Further studies are needed to clarify the relationship between histopathology and FDG uptake in the thymus.

A cancer screening system using positron emission tomography (PET) was established in Japan to detect asymptomatic malignancies in healthy subjects. A description of this system has been presented [1, 2] and details have recently been made available [3]. Based on our experience, we have reported the occurrence of non-pathological fluorine-18 fluorodeoxyglucose (FDG) uptake [4].

Thymic uptake is a known cause of non-pathological FDG uptake [5]. This uptake seems to disappear after puberty owing to progressive fatty infiltration of the thymus [6]. However, the small number of patients studied to date has provided only limited knowledge of the incidence and characteristics of this uptake.

Our cancer screening system included performing FDG-PET and CT on participants, providing the opportunity to compare FDG-PET and CT findings of the thymus. This study focuses on persons below 30 years of age because it has been reported that below this age the thymus is recognizable on CT in 100% of cases [7]. The correlation between thymic FDG uptake and CT attenuation of the thymus (CAT) was investigated.

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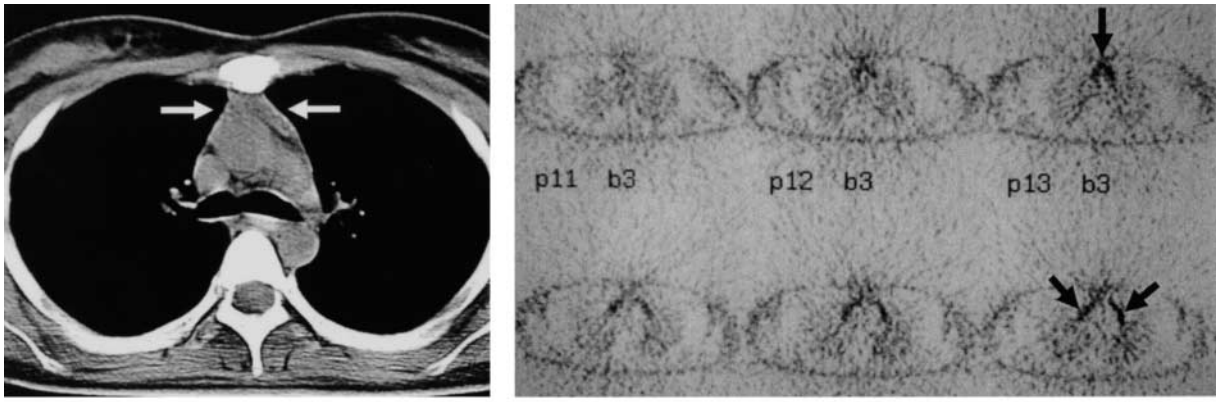
## Materials and methods

Our cancer screening system was approved by the Ethical Committee of the HIMEDIC Imaging Center at Lake Yamanaka. After a detailed explanation of the examination process, written informed consent was obtained from all participants. 94 Japanese subjects below 30 years of age with a morphologically normal thymus were selected from all participants involved in this screening system from January 1995 to March 2000. A thoracic surgeon (NN) diagnosed a normal thymus on the basis of CT appearance (Figure 1a), as demonstrated in previous reports [7–11]. No subject had any clinical symptoms suggestive of thymus-related diseases, such as myasthenia gravis and other immunological disorders, or mediastinal tumours before September 2000 (follow-up period 6–69 months).




(a) (b)

**Figure 1.** (a) CT and (b) transaxial fluorine-18 fluorodeoxyglucose positron emission tomography (FDG-PET) images at the level of the superior mediastinum in a subject with positive PET findings. (a) The thymus appears to be morphologically normal (arrows). (b) Wedge-shaped FDG uptake is noted (arrows).

PET scans were performed on an ECAT EXACT47 whole body PET system (Siemens/CTI, Knoxville, TN). 260–370 MBq (7–10 mCi) of FDG was administered intravenously after the subjects had fasted for at least 5 h. A 35 min static emission scan was performed in five different bed positions, including the level of the chest. The transaxial resolution was 6.0 mm full-width at half maximum. A series of 47 transaxial slices per scan position, with 3.3 mm thickness, were reconstructed on a $128 \times 128$ matrix. Transmission scanning for attenuation correction was not performed.

Thymic uptake was visually assessed by two independent investigators (HF, MI) without knowledge of the CT findings. The presence of concave or wedge-shaped tracer accumulation in the anterior mediastinum was the criterion for a positive scintigram (Figure 1b). Disagreements between the two investigators were resolved by a third investigator (TN) blinded to the previous interpretations to achieve consensus. The count ratio between the thymus and the lung (T/L ratio) was calculated as a semi-quantitative index [12, 13]. The thymic uptake count was measured with a square region of interest (ROI) (6.9 mm per side), placed on the area corresponding to the mid portion of the uptake site by another investigator (AS). Lung uptake counts were measured on the same slice as the thymic uptake count, with two square ROIs (6.9 mm per side) placed over the centre of the lungs. The average of the two lung uptake counts from both sides was used.

Non-contrast enhanced spiral CT of the chest was performed on all subjects using a Super Helix TCT 900S unit (Toshiba, Tokyo, Japan). 10 mm thick contiguous transaxial CT images were obtained at a peak voltage of 120 kV and a tube current of 150 mA at 1 s per slice. To calculate the CAT value, a square ROI (7.5 mm per side) was placed on the mid portion of the anterior mediastinum. CAT was expressed as Hounsfield units (HUs).

Linear regression analyses were performed to obtain the correlation of the T/L ratio with CAT value and age. Correlation between the T/L ratio and the body mass index (BMI) was also evaluated because of the necessity to investigate the effects of attenuation on the presence of thymic uptake in non-attenuation corrected images.

## Results

The mean age of the 94 subjects was 25.4 years (range 18–29 years). The chest CT showed normal lungs in all subjects. 32 (34%) of the 94 thymuses had increased FDG uptake. In these 32 cases, the T/L ratio was $2.86 \pm 0.49$ (range 2.02–3.99). Thymic uptake could not be identified and the T/L ratio could not be measured in the remaining 62 cases. 86 (91%) of the 94 thymuses were available for calculating the CAT value, including all of the 32 subjects with positive PET findings. In these 86 cases, the CAT value was $-17.5 \pm 45.7$ HU (range –103.6 HU to 79.9 HU). The CAT value could not be measured in the remaining eight cases owing to the narrowness of the anterior mediastinum.

The T/L ratio correlated with the CAT value (Figure 2). There was no correlation between the T/L ratio and BMI ($p=0.87$) or age ($p=0.13$). The CAT value in subjects with positive PET findings was significantly higher than in subjects with negative PET findings (Figure 3) ($22.4 \pm 31.7$ HU *vs* $-41.0 \pm 35.2$ HU; $p<0.001$, unpaired *t*-test).

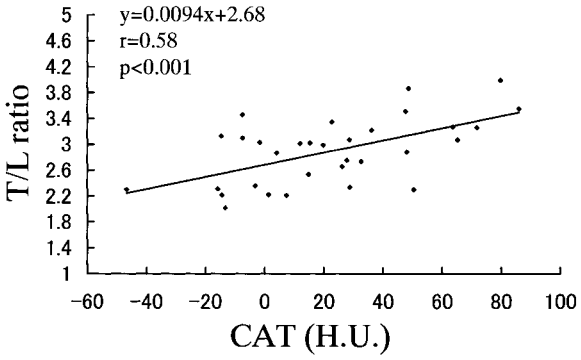



**Figure 2.** Scatterplot of CT attenuation values of the thymus (CAT) against the thymus to lung ratio (T/L ratio) in fluorine-18 fluorodeoxyglucose positron emission tomography.

## Discussion

FDG-PET offers information regarding tissue glucose metabolism and detects hypermetabolic tissue. Increased FDG uptake is seen not only in malignancies but also in normal organs, which is referred to as "physiological or non-pathological FDG uptake". It is important to understand physiological thymic uptake, since thymic uptake with false positive findings may lead to the performance of unnecessary additional examinations [14–16].

Concern has focused on the period of diminution of this uptake in order to avoid misinterpretation of physiological thymic uptake. Patel et al [6] and Brink et al [16] suggested that physiological thymic uptake can be observed in childhood until the onset of puberty, although we observed increased thymic uptake and normal CT findings in young adults. Since their studies did not include healthy young subjects, evaluation of the characteristics of thymic uptake could be insufficient. We believe that physiological thymic uptake can be seen in some young adults for the following reasons: (a) the relationship of thymic uptake with known morphological and immunological changes of the thymus [6, 16]; (b) decrease in the CAT value owing to increasing atrophy of the thymic tissue associated with fatty infiltration of the thymus [17]; and (c) the thymus could be detected below the age of 30 years by CT in 100% of cases in the study by Baron et al [7]. In other words, if the morphology and metabolic activity of the normal thymus are correlated, physiological thymic uptake in young adults below the age of 30 years can be depicted on FDG-PET. We therefore investigated the relationship between CAT and thymic FDG uptake in such persons. Correlation was found between the T/L ratio and the CAT value. The CAT ranges within our group were very large (Figure 3), consistent with the fact that morphological changes of the thymus during life vary in degree depending on the individual [17]. These results led us to speculate that some of our subjects may have had a relatively slow fatty infiltration in the thymus, resulting in the depiction of thymic FDG uptake by residual, non-infiltrated thymic parenchyma. Histopathological investigation will therefore be required to clarify the correlation between metabolic activity as shown by FDG accumulation and thymic tissue density as shown by the CAT value.

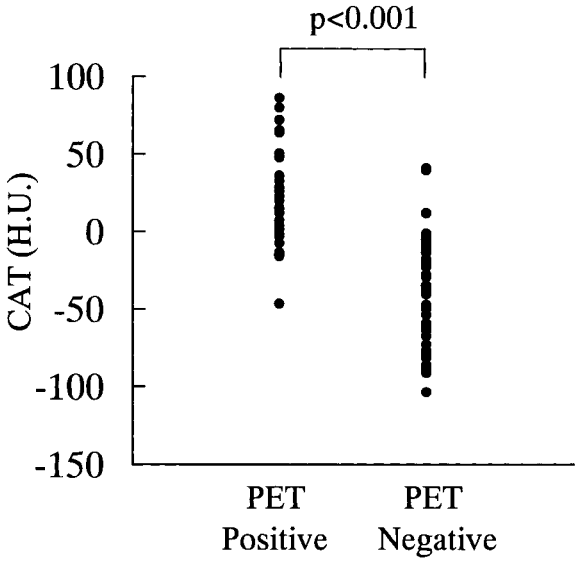



**Figure 3.** Comparison of the CT attenuation values of the thymus (CAT) and positron emission tomography (PET) findings.

Increased thymic uptake in some young adults may possibly be due to pathological conditions. Several mediastinal tumours have shown increased uptake on FDG-PET and it is difficult to differentiate between benign and malignant thymic tumours [18, 19]. CT findings may be non-specific for detecting thymic disorders such as thymic hyperplasia [20], although our selected subjects had normal findings on CT images. Furthermore, patients with slow-growing mediastinal tumours may remain asymptomatic for a long time. However, it would be unlikely that all of the 32 thymuses with increased FDG uptake were pathological in nature.

We did not study participants over 29 years of age because the PET results were negative in almost all such persons and the CT images were unavailable or it was very difficult to calculate the CAT value. To our knowledge, no subject older than 30 years of age with no evidence of malignancy and a positive FDG-PET finding (false positive) has been reported. Physiological thymic uptake may therefore be unusual in healthy older persons. By contrast, systemic treatment such as chemotherapy [16] and radioiodine therapy [21] have been reported as inducing thymic uptake even in older patients. In this

respect, knowledge of not only the patient's age but also their medical history is needed when interpreting thymic uptake in FDG-PET.

In summary, we suggest caution in interpreting our results because of the lack of histopathological evidence. Further studies are necessary to elucidate the incidence and significance of physiological thymic FDG uptake. However, our results suggest that even in adults, if the thymus has a relatively high CT attenuation value, the presence of physiological thymic uptake on FDG-PET is a normal variant.

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