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## Clinical usefulness of FDG–PET/CT for the evaluation of various types of adult T-cell leukemia

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### ABSTRACT

**Purpose:** The aim was to explore undefined useful indices for clinically grading adult T-cell leukemia (ATL) using [<sup>18</sup>F] 2-fluoro-2-deoxyglucose (FDG) – positron emission tomography/computed tomography (PET/CT).

**Methods:** A total of 28 patients with ATL (indolent, 9; aggressive, 19) were enrolled; all patients with aggressive ATL underwent FDG–PET/CT before chemotherapy. Patients with indolent ATL underwent FDG–PET/CT at the time of suspected disease progression and/or transformation; some received lymph node biopsy. The quantitative parameters maximum standardized uptake values (SUVmax), and mean and peak SUV, metabolic tumor volume (MTV), and volume-based total lesion glycolysis were calculated with the margin threshold as 25%, and 50% of the SUVmax for all lesions.

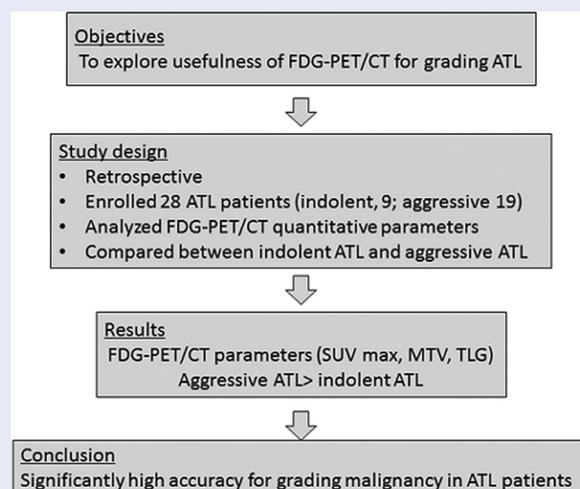
**Results:** All parameters except for MTV-25% showed significant differences ( $P \leq 0.05$ ) in differentiating the aggressive type from the indolent type of ATL. Areas under the curve for receiver-operating characteristic (ROC) analysis regarding the series of parameters investigated ranged from 0.75 to 0.92; this indicated relatively high accuracy in distinguishing the aggressive type from the indolent type. No malignant findings were detected in lymph node biopsies in indolent ATL patients with lymphadenopathy.

**Discussion:** We performed evaluation of a line of parameters of FDG–PET, thereby demonstrating their significantly high accuracy for grading malignancy in ATL patients. In particular, low accumulation of FDG in indolent ATL patients with lymphadenopathy might predict that it is not a sign of disease transformation, but rather a reactive manifestation.

**Conclusion:** FDG–PET/CT findings could be useful for clinically grading ATL.

### KEYWORDS

Adult T-cell leukemia; indolent type; aggressive type; positron emission tomography; standardized uptake value; metabolic tumor volume; total lesion glycolysis; volume-based parameter



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## Introduction

Patients with aggressive adult T-cell leukemia (ATL) (i.e. acute, lymphoma and unfavorable chronic types) require intensive treatment, whereas those with indolent ATL (i.e. favorable chronic and smoldering) need mild management as a subtype of chronic lymphoid leukemia [1,2]. Patients with indolent-type ATL usually exhibit skin lesions and/or leukocytosis with increased levels of abnormal lymphocytes, but show no lymphadenopathy or involvement of organs other than skin or lung. Most patients with indolent ATL are treated with watchful waiting until disease progression to acute crisis. We sometimes find patients with indolent ATL with lymphadenopathy, which represents suspected signs of disease progression and/or transformation; lymph node biopsy is usually performed for accurate diagnosis. In these patients, histologically proven ATL-involved lymphadenopathy or other ATL lesions (pleural effusion, ascites or involvement of CNS, bone, gastrointestinal tract, liver or spleen) are required for diagnosis of acute-type ATL.

Diagnostic imaging plays a critical role in clinical staging and evaluation of efficacy in patients with malignant lymphoma [3,4]. In particular, [<sup>18</sup>F] 2-fluoro-2-deoxyglucose (FDG)-positron emission tomography (PET) provides considerable information relative to other imaging modalities such as CT and <sup>67</sup>Ga scintigraphy. FDG-PET is widely used to predict prognosis in solid malignancies including lung, and head and neck carcinomas [5]. FDG uptake in aggressive non-Hodgkin's lymphoma (NHL) is significantly higher than in indolent lymphoma, and standardized uptake values (SUV) are helpful in distinguishing between indolent and aggressive NHL [6]. Furthermore, recent improvements in FDG-PET/CT software allow measurement of disease burden indicators, such as metabolic tumor volume (MTV) and total lesion glycolysis (TLG) [5,7]. MTV is measured by a semiautomatic software with an automatic iso-contour threshold algorithm. TLG is also a volume-based parameter, shown to be a promising prognostic index in various malignancies including malignant lymphoma [8,9]. However, intensive analyses of FDG-PET in ATL patients have not been fully reported.

The purpose of the present study was to explore the potential relationship between malignant grade and analytical values as assessed using PET/CT volumetric techniques including SUV, MTV and TLG.

## Materials and methods

### Patients

Twenty-eight patients diagnosed with ATL (nine with smoldering or chronic, and 19 with lymphoma or acute types) were enrolled. All patients underwent

skin ( $n = 14$ ) or lymph node ( $n = 6$ ) biopsies or hematological diagnosis from peripheral blood ( $n = 13$ ). Patients received <sup>18</sup>F-FDG PET/CT between July 2013 and November 2015. Evaluation of clinical stage included complete blood count, biochemistry, chest X-ray, CT scans of the neck, chest and abdomen, FDG-PET/CT, and bone marrow examination. The present study was approved by the institutional review board at our university hospital (approval number 800), and all participants gave written informed consent.

### FDG-PET and image analysis

A PET/CT scanner (Biograph mCT, Siemens Healthcare, Erlangen, Germany) with time-of-flight (TOF) was used in the present study. The image analysis was performed using a workstation with syngo-via software (Siemens Healthcare, Erlangen, Germany). CT scanning parameters were as follows: peak X-ray tube voltage, 120 kVp; tube current, automatic exposure control (care dose 4D), 90 mAs; field of view, 50 × 50 cm; and beam width, 1.2 mm × 32. Whole-body PET/CT images were acquired at 1 hour after intravenous injection of 3.7 MBq of FDG per 1 kg body weight (upper limit, 340 MBq); an emission scan was obtained from the top of the skull to the upper thigh or soles of the feet, for 120 s/bed per field of view each covering 92.88 mm, at an axial sampling thickness of 2 mm/slice (1 bed position 216 mm; each covering). Peak SUV (SUV<sub>peak</sub>) [10] was defined as the average SUV within a small, fixed-size region of interest (ROI<sub>peak</sub>) centered on a high-uptake region of the tumor. Values of maximum SUV (SUV<sub>max</sub>) and TLG with two variable margin thresholds were also acquired for analysis. TLG of a target lesion was calculated as the mean SUV (SUV<sub>mean</sub>) × MTV, which considers both the metabolic activity and tumor burden. SUV<sub>mean</sub> was measured by setting margin thresholds of 25%, and 50% of SUV<sub>max</sub> for each lesion, resulting in SUV<sub>mean</sub>-25%, and SUV<sub>mean</sub>-50%, respectively. MTV was also measured by setting the margin thresholds as 25%, and 50% of SUV<sub>max</sub> for each lesion, resulting in TLG-25% and TLG-50%, respectively. We estimated the MTV using a threshold method based on 25%, and 50% of SUV<sub>max</sub>, as proposed by Ceriani et al. [11] and by Boellard et al. [12] for evaluation of tumoral lesions. On a patient basis, SUV<sub>max</sub> was defined as the highest SUV<sub>max</sub> among those for all lesions, and TLG for a patient was defined as the sum of all those lesions.

### Statistical analysis

Between-group differences in PET parameters were evaluated using Fisher's exact test and Student's *t*-test as appropriate. Two sided *P* values <0.05 were

considered as significant. All statistical analyses were performed using EZR (Saitama Medical Centre, Jichi Medical University, Saitama, Japan), a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria, version 2.13.0). More precisely, it is a modified version of R commander (version 1.27) that was designed to add statistical functions frequently used in biostatistics [13]. Receiver-operating characteristic (ROC) analyses were undertaken to assess the utility of PET/CT parameters for stratifying malignancy grade. Optimal cut-off values were identified by determining the values where the sum of sensitivity and specificity was maximal. Two nuclear medicine radiologists (Y.A. and M.O.) assessed the presence or absence of each lesion (qualitative analysis). Inter-observer agreement on FDG-PET/CT findings were analyzed using weighted  $\kappa$  statistics, defined as poor ( $\kappa < 0.2$ ), fair ( $0.2 < \kappa \leq 0.4$ ), moderate ( $0.4 < \kappa \leq 0.6$ ), good ( $0.6 < \kappa \leq 0.8$ ), and very good ( $0.8 < \kappa \leq 1$ ) [14]. These analyses were performed for all nodal regions.

## Results

### Characteristics of patients studied

The clinical and pathologic characteristics of the 28 patients with ATL are shown in Table 1. Each patient's ATL subtype was determined according to Shimoyama criteria [1], which are internationally accepted for classification of ATL subtype. All patients with aggressive ATL (lymphoma 7, acute-type 12) underwent FDG-PET/CT scans prior to chemotherapy. Patients with indolent ATL (smoldering 6, chronic 3) underwent at the time of suspected disease progression and/or transformation. Among them, two patients underwent

**Table 1.** Characteristics of the 28 patients with ATL.

Characteristic	No.	%
Age, years		
Median	63.5	
Range	37–81	
Subtype		
Acute type	12	42.9
Lymphoma type	7	21.4
Chronic type	3	10.7
Smoldering type	6	21.4
Performance status		
0–1	20	71.4
2–4	8	28.6
LDH, IU/L		
Median	303	
Range	147–1050	
LDH>2×ULN	11	
Soluble IL-2R		
Median	4399	
Range	215–75000	
Number of extra-nodal sites		
0–1	17	60.7
2 or more	4	14.3
Clinical stage (Ann Arbor staging)		
I–II	2	7.1
III–IV	26	92.9

Abbreviations: ATL: adult T-cell leukemia; LDH: lactate dehydrogenase; IL-2R: interleukin-2 receptor.

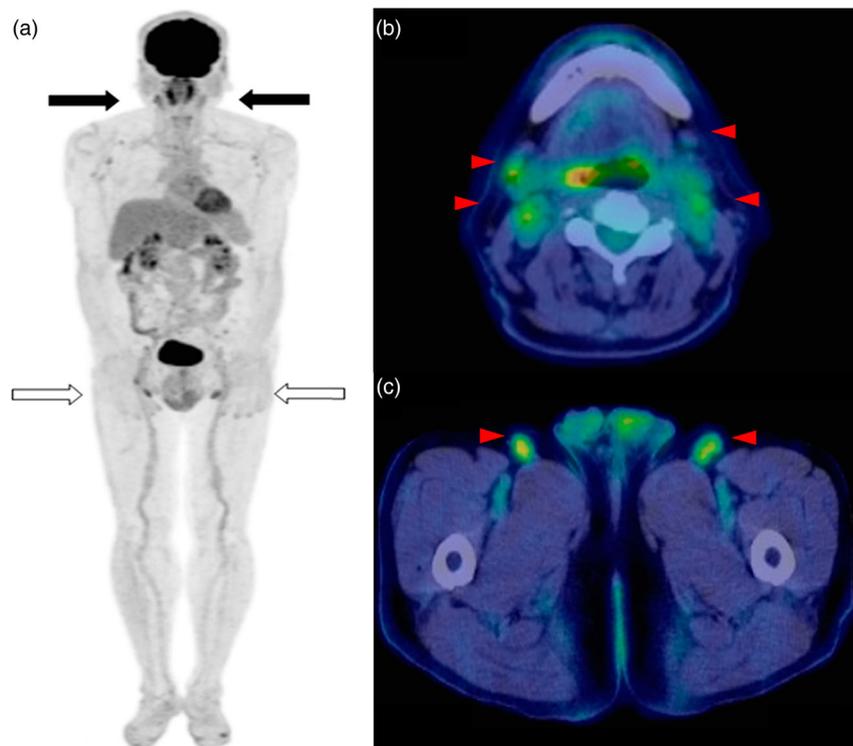
FDG-PET/CT scans when they relapsed. One patient with the chronic type received chemotherapy at 4 months before PET/CT, and another patient with the acute type received umbilical-cord blood transplantation at 6 months before PET/CT. The median age was 63.5 (range, 37–81) years with a male:female ratio of 1:1. Nineteen of the 28 patients had aggressive ATL (lymphoma, acute). Twenty of the 28 patients had a low performance status score (0–1). Twenty-six patients were categorized as being at an advanced clinical stage (III–IV). In 12 patients, FDG-PET/CT was performed from the top of the skull to the upper thigh. In the other patients, FDG-PET/CT was performed from the top of the skull to sole of the feet.

All the nine patients with indolent ATL underwent FDG-PET/CT at a time when they showed lymphadenopathy; this is a suspected sign of disease progression and/or transformation. Lymph node biopsy was performed in six of these patients; however, pathological findings were HTLV-I associated lymphadenitis or dermatopathic lymphadenitis, which were reactive disorders [15,16].

### Parameters for glucose metabolism in all lesions

A representative patient with indolent ATL exhibited low accumulation of FDG (Figure 1), whereas a representative patient with aggressive ATL showed apparently higher accumulation of FDG (Figure 2). The median PET/CT parameters of all target lesions before treatment or at the time of suspected disease progression are listed in Table 2. FDG-avid lesions and parameters in each patient are detailed in Table 3. All patients except one showed FDG uptake in lymph nodes, and some had FDG-avid extra-nodal lesions such as in the spleen, skin, bone and liver. Patient 22 had chronic-type ATL, with higher SUVmax and 50% TLG than the rest of the indolent group, and showed systemic lymphadenopathy, splenomegaly, fever and liver dysfunction. A lymph node biopsy showed reactive lymphadenitis. As this patient was suspected of having chronic active Epstein-Barr virus infection (CAEBV) because of high peripheral levels of anti-EBV VCA-IgG, EBV-EA IgG, and EBV-DNA in peripheral blood, we considered that high FDG accumulation in this patient might reflect CAEBV activity [17].

All of the pertinent parameter values for aggressive ATL were significantly higher than those for indolent ATL (Table 4). In patients with indolent ATL, FDG accumulation of the chronic type was higher than that of the smoldering type, albeit that there was no statistical difference (Table 2). ROC analyses were performed to evaluate the usefulness of each PET/CT parameter in discriminating malignant grade. The AUC in ROC analysis of SUV, MTV and TLG ranged from 0.75 to 0.9, indicating high accuracy (Table 5).



**Figure 1.** 2-Fluoro-2-deoxyglucose (FDG)-positron emission tomography/computed tomography (FDG-PET/CT) imaging of a 64-year-old male with representative indolent adult T-cell leukemia (ATL) of the smoldering type. (A) FDG-PET, maximum intensity projection (MIP), whole-body image. Images show neck (black arrows) and inguinal lymph nodes (empty arrows). (B) Cervical region (red arrow-heads) of integrated PET-CT axial view. (C) Inguinal region (red arrow-heads) of integrated PET-CT axial view. A typical indolent case was selected. MIP of FDG-PET shows multiple lesions (neck and inguinal regions) as low accumulations of FDG (A). The cervical plane depicts low accumulations of FDG in bilateral submandibular (SUVmax, 3.85) and deep internal jugular lymphadenopathies (SUVmax, 4.31) (B), and bilateral inguinal regions (SUVmax, 4.73) (C).

### Inter-observer agreement

The two nuclear medicine radiologists' inter-observer agreement for presence or absence of lesions shown by FDG-PET/CT is detailed in Table 6. The  $\kappa$  value for all nodal regions was 0.97, indicating good inter-observer agreement ( $\kappa > 0.4$ ). Their  $\kappa$  values for individual nodal regions were also satisfactory.

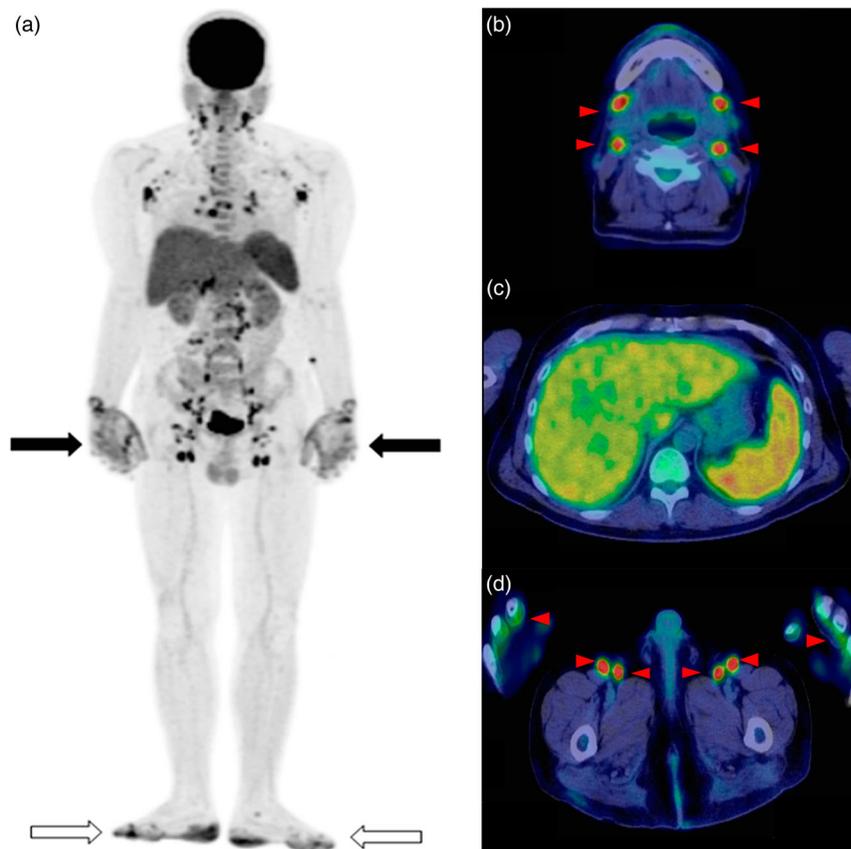
### Discussion

The present study demonstrated that the PET/CT parameters (SUV, MTV and TLG) investigated were useful predictors of grade of malignant tumor in ATL patients. We analyzed the clinical utility of PET/CT parameters in distinguishing indolent ATL from aggressive ATL. A series of PET/CT parameter values (SUVmax, SUVpeak, SUVmean-25%, SUVmean-50%, MTV-25%, MTV-50%, TLG-25% and TLG-50%) for aggressive ATL were significantly higher than those for indolent ATL. It was also demonstrated that the AUC for these PET/CT parameters ranged from 0.75 to 0.92, indicating high accuracy in distinguishing indolent ATL from aggressive ATL. These results demonstrate that a series of PET/CT parameters other than SUVmax are also clinically-useful parameters comparable to SUVmax in evaluating the malignancy grade of ATL. Our results also

clearly demonstrated that overall inter-observer agreement between FDG-PET/CT findings was excellent.

In FDG-PET/CT, FDG uptake and subsequent hyper-metabolism of glucose is a reliable surrogate marker of aggressive biology in solid tumors and lymphomas [4,18]. SUV has been used as a quantitative parameter for glucose metabolism, and SUVmax for a tumor lesion has been widely used as a survival predictor or in the grading of several solid tumors and some lymphomas [5,8,9]. However, it should be noted that SUVmax reflects the metabolic activities of the most aggressive cells, which does not necessarily align with the prognostic index. In some malignancies, TLG has recently been suggested as being a better metabolic parameter than SUVmax in FDG-PET/CT because TLG reflects the metabolic tumor burden [7]. Among a variety of malignant lymphomas, Hodgkin lymphoma and diffuse large B-cell lymphoma show a high level of FDG uptake, indicating representative 'FDG-avid lymphomas' [3]. In contrast, other studies have demonstrated lower rates of PET detection for cutaneous T-cell lymphoma and extra-nodal marginal zone lymphoma [19]. However, there have been very few reports concerning FDG-PET studies on ATL [20–25].

ATL is notably characterized by multiple tumor lesions, which indicate a large tumor burden leading to multiple-organ failure [1]. We therefore



**Figure 2.** 2-Fluoro-2-deoxyglucose (FDG)-positron emission tomography/computed tomography (FDG-PET/CT) imaging of a 56-year-old male with representative acute-type aggressive adult T-cell leukemia (ATL). (A) FDG-PET maximum intensity projection (MIP) whole-body image. Images show subcutaneous regions of hands (black arrows) and soles of the feet (empty arrows). (B) Cervical region (red arrow-heads) of integrated PET-CT, axial view. (C) Hepatic and splenic regions of integrated PET-CT, axial view. (D) Inguinal region (red arrow-heads) of integrated PET-CT, axial view. (A) A typical aggressive case was selected. This case shows several lymphadenopathy, hepatomegaly, splenomegaly, and skin lesions. MIP of FDG-PET shows multiple lesions (neck, axilla, mediastinum, para-aorta, iliac, inguinal lymph node regions, liver, spleen and subcutaneous regions of the hand and planta) as high accumulations of FDG (A). The cervical plane depicts high accumulations of FDG in bilateral submandibular (SUVmax, 10.16) and deep internal jugular (SUVmax, 8.56) lymphadenopathies (B), liver (SUVmax, 7.92) and spleen (SUVmax, 8.55) (C), bilateral inguinal (SUVmax, 6.51) and palmar subcutaneous regions (SUVmax, 6.51) (D).

**Table 2.** PET/CT parameters according to ATL type.

Parameter	Indolent		Aggressive	
	Smoldering Median (range)	Chronic Median (range)	Lymphoma Median (range)	Acute Median (range)
SUVmax	4.6 (1.9–7.6)	6.6 (3.1–14.6)	17.0 (6.0–27.9)	14.1 (6.6–41.6)
SUVpeak	3.1 (1.9–5.36)	5.1 (2.6–13.3)	10.9 (3.3–23.0)	11.1 (3.9–31.4)
SUVmean25%	2.0 (0.97–3.4)	3.5 (1.4–6.4)	6.7 (2.4–12.9)	6.9 (2.8–21.7)
SUVmean50%	3.0 (1.3–5.2)	4.6 (2.3–11.7)	11.9 (4.0–17.6)	10.1 (4.5–28.9)
MTV25%	70.4 (10.1–470.6)	174.4 (34.1–123.2)	325.0 (18.7–740.8)	383.6 (78.1–1772)
MTV50%	11.6 (4.9–91.2)	48.3 (28–52)	82.8 (2.62–151.1)	97.8 (28–397.1)
TLG25%	130.2 (8.0–483.2)	319.5 (103.5–749.2)	982.4 (72.3–2776.5)	1565 (193–4606.8)
TLG50%	34.1 (5.7–129.4)	89.2 (83–307.7)	208 (16.7–1325.3)	607 (90–2778.3)

Abbreviations: SUV: standardized uptake value; MTV: metabolic tumor volume; TLG: total lesion glycolysis.

hypothesized that TLG could help evaluate tumor burden and extent in ATL patients. The present study suggests that TLG, which reflects total metabolic tumor volume, also reflects aggressiveness and SUVmax in ATL (Table 5). MTV and TLG are immediately measured after ROI placement on the lesion by PET software, and facilitate measurement of lesion volume. As expected, our data demonstrates that

both the intensity of FDG uptake and metabolic volume were significantly lower in the indolent type relative to the aggressive type (Table 4), even though all the patients with the indolent type underwent FDG-PET/CT at the time when we suspected disease progression and/or transformation in these patients. We could not compare advantages of TLG with other FDG-PET parameters in the current study due to the

**Table 3.** The profile of FDG-avid lesions and parameters in each patient.

	Age	Gender	Type	Stage	Lesion of FDG uptake	SUVmax	50%TLG
1	70	M	Acute	IV	L/N, mediastinal tumor	15.68	749.1
2	60	F	Acute	IV	L/N, lung, spleen	6.56	164.8
3	52	F	Acute	IV	L/N, spleen, liver	13.69	181
4	69	F	Acute	IV	L/N, liver, skin, stomach orbital tumor, muscle	32.45	1094.1
5	64	F	Acute	IV	lung, intestine	14.61	2778.3
6	37	M	Acute	IV	L/N, spleen, bone	39.84	447.6
7	67	F	Acute	IV	L/N	11.29	90
8	63	M	Acute	IV	L/N, skin	23.41	801.6
9	69	F	Acute	IV	L/N, lung, bone	9.03	464.7
10	56	M	Acute	III	L/N, spleen	6.73	802
11	72	F	Acute	IV	L/N, spleen, bone	41.6	227.4
12	56	M	Acute	IV	L/N, skin, liver, spleen	12.99	1656
13	76	M	Lymphoma	III	L/N	27.89	1138.2
14	63	M	Lymphoma	IV	L/N, skin	19.63	1325.3
15	63	M	Lymphoma	IV	L/N, spleen, CNS	23.79	1214.1
16	66	M	Lymphoma	II	L/N	5.99	43.5
17	73	F	Lymphoma	III	L/N	16.99	208
18	78	M	Lymphoma	IV	L/N, skin	11.8	27.1
19	69	F	Lymphoma	II	L/N	10.4	16.7
20	47	F	Chronic	III	L/N	3.06	83
21	55	M	Chronic	III	L/N, spleen	6.61	39.2
22	61	F	Chronic	III	L/N, spleen	14.55	307.7
23	59	F	Smoldering	IV	L/N	7.56	59.5
24	59	F	Smoldering	IV	L/N	1.86	5.67
25	43	M	Smoldering	II	L/N	4.89	12.6
26	81	F	Smoldering	IV	L/N, skin	2.41	129.4
27	64	M	Smoldering	IV	L/N, skin	4.73	18.9
28	76	M	Smoldering	III	L/N	4.46	49.2

Abbreviations: SUV: standardized uptake value; TLG: total lesion glycolysis; L/N: lymph node; CNS: central nervous system.

relatively few subjects. Further studies with larger cohorts are required, both to verify our findings, and to elucidate the usefulness of TLG in predicting prognosis and aggressive transformation in patients with ATL.

We also used PET-CT to optimize selection of biopsy sites in patients with suspected disease transformation, by targeting lymph nodes with the highest SUVmax values. It should be noted that there was concordance between low FDG/PET parameter values and no malignant pathological findings from lymph node biopsy. These findings suggest that low positive FDG/PET parameters in indolent ATL patients with lymphadenopathy might predict that it is not a sign of disease

**Table 4.** Comparisons of PET parameters according to malignant grade.

Parameter	Indolent (n = 10)	Aggressive (n = 18)	P value
SUVmax average (SD)	5.6 (±3.8)	17.8 (±11.0)	0.003
SUVpeak average (SD)	4.4 (±3.6)	13.0 (±8.2)	0.006
SUVmean25% average (SD)	2.6 (±1.7)	8.1 (±5.1)	0.004
SUVmean50% average (SD)	3.8 (±2.6)	12.4 (±7.3)	0.002
MTV25% average (SD)	168.8 (±174.8)	490.9 (±398.9)	0.07
MTV50% average (SD)	27.7 (±28.6)	130.7 (±118.4)	0.02
TLG25% average (SD)	265.2 (±254.7)	1672.5 (±1460.8)	0.008
TLG50% average (SD)	84.0 (±93.1)	706.8 (±711.9)	0.02

Abbreviations: SUV: standardized uptake value; MTV: metabolic tumor volume; TLG: total lesion glycolysis; SD: standard deviation.

transformation from indolent type to aggressive type, but rather a reactive manifestation.

In the present study, we endeavored to optimize the margin threshold for both MTV and TLG measurements. It is widely accepted that the optimal margin threshold has not been established [11,12]. Therefore, we assessed two margin thresholds, 25 and 50%. There was no difference in margin thresholds between 25 and 50% except for the MTV-25% (Tables 4 and 5). In calculating MTV, a high threshold

**Table 5.** Area under the curve obtained using receiver-operating characteristic curve analysis.

Parameter	AUC	95%CI	P value
SUVmax	0.91	0.79–1.00	–
SUVmean25%	0.90	0.78–0.99	0.53
SUVmean50%	0.92	0.81–0.99	0.69
SUVpeak	0.89	0.76–1.00	0.41
MTV25%	0.75	0.55–0.94	0.12
MTV50%	0.81	0.65–0.97	0.25
TLG25%	0.83	0.69–0.99	0.27
TLG50%	0.85	0.71–1.0	0.35

Abbreviations: SUV: standardized uptake value; MTV: metabolic tumor volume; TLG: total lesion glycolysis; AUC: area under the curve; CI: confidence interval.

Note: The AUC of the SUVmax was compared for each parameter.

**Table 6.** Inter-observer agreement for qualitative analysis of lesions shown by FDG-PET/CT.

Parameter	κ
All nodal regions	0.97
Nodal regions	
Cervical	0.906
Supraclavian	0.976
Mediastinal	0.965
Abdominal	0.941
Pelvic	0.953
Spleen	1.000

tends to underestimate tumor burden, and a low threshold tends to overestimate tumor burden.

The present study had some limitations. First, analytical methods may fail to detect malignancy-associated FDG accumulation in skin lesions, peripheral blood and intestine lesions, partly because physiological or pathophysiological accumulation independent of malignancies may interfere; in addition, very small lesions may be below the limits of spatial resolution. Even though skin invasion by ATL was proven by biopsy, FDG uptake would not be detected in some cases. In the present study, 14 of 28 patients had skin lesions. Although their PET images were negative, skin lesions were proven by biopsy in 7 of 14 patients with skin lesions. It is therefore possible that a false-negative would be attributed to the flatness of the lesions as well as to earlier disease stage. Second, the number of ATL patients in this study was not large. We therefore could not ascertain optimal cut-off values for PET/CT parameters to differentiate between aggressive and indolent ATL types. Further studies with larger study cohorts are needed to verify and enlarge on our findings, particularly the relationship between FDG-PET/CT parameters and prognosis among aggressive ATLs.

Third, although patients in whom ATL was suspected to have transformed from indolent to aggressive type underwent FDG-PET/CT, their uptake was low, which suggests that FDG uptake in indolent types may be reactive.

Fourth, due to the small number of patients, FDG PET/CT parameters overlapped at the lower end of the aggressive group and the upper end of the indolent group.

In summary, the present study showed some PET-CT parameters – SUV, MTV, and TLG – were accurate indicators of malignancy grade in patients with ATL; and that related FDG-PET parameters can potentially indicate need and optimal biopsy site for patients in whom ATL progression or transformation is suspected.

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## Disclosure statement

The authors declare that they have no conflict of interest.

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