

# **$^{18}\text{F}$ -FDG PET/CT characteristics of pulmonary sclerosing hemangioma vs. pulmonary hamartoma**

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**Abstract.** The radiological features of pulmonary sclerosing hemangioma (PSH) and pulmonary hamartoma are poorly specified. Thus, the present study aimed to compare and analyze the characteristics of fluorodeoxyglucose positron emission tomography/computed tomography ( $^{18}\text{F}$ -FDG PET/CT) in PSH versus pulmonary hamartoma.  $^{18}\text{F}$ -FDG PET/CT characteristic findings of 12 patients with PSH and 14 patients with pulmonary hamartoma were retrospectively reviewed. A total of 12 lesions were detected from the 12 patients with PSH, of which 3 masses exhibited calcification. The mean diameter and standardized maximum uptake value (SUVmax) were  $1.9 \pm 0.7$  cm and  $2.6 \pm 1.0$ , respectively, and there was no significant correlation between the lesion size and SUVmax ( $P > 0.05$ ). For the 14 patients with pulmonary hamartoma, 14 lesions were found, of which 4 exhibited calcification. The mean diameter and SUVmax were  $1.7 \pm 0.8$  cm and  $1.5 \pm 0.6$ , respectively, and there was a significant correlation between the size and SUVmax ( $r = 0.625$ ,  $r^2 = 0.391$ ,  $P < 0.05$ ). Although there was no significant difference between the size of PSH and pulmonary hamartoma ( $P > 0.05$ ), the SUVmax of PSH was significantly higher than that of pulmonary hamartoma ( $P < 0.05$ ). Moreover, the SUVmax of 1.95 was applied as a cutoff for the diagnosis of PSH, and the resulting sensitivity and specificity for PET/CT to differentiate PSH from pulmonary hamartoma were 83.3 and 78.6%, respectively. Although the morphological features were not specific, PSH showed significantly higher FDG accumulation than pulmonary hamartoma on PET/CT imaging, which may aid the differential diagnosis. Further studies with larger populations are warranted to confirm these study results.

## **Introduction**

Pulmonary hamartoma is the most common benign tumor of the lung, accounting for ~75% of all pulmonary benign tumors. Pulmonary sclerosing hemangioma (PSH), which originates from type II pneumocytes, is a rare lung tumor, accounting for 3-5% of benign lung lesions. Pulmonary hamartoma and PSH usually present as a well-defined, peripheral, solitary lung nodule or mass on computed tomography (CT) examination, and calcification may occasionally be present (1-6). These morphological features are not specific enough to differentiate the lesions from other pulmonary tumors. Fluorodeoxyglucose positron emission tomography/CT ( $^{18}\text{F}$ -FDG PET/CT), which can provide morphological and metabolic information on tumors, has been reported to be useful in differentiating benign pulmonary tumors from malignancies. Usually, benign lung tumors display a lack of metabolic activity or light to moderate FDG uptake on PET/CT, which corresponds to their slow-growing behavior (7,8).

However, a few studies have suggested that certain benign pulmonary tumors, such as PSH, may be low-grade malignancies, since cases of lymph node and lung metastases have been reported (9-14), or that the malignant transformation of lung benign tumors may be possible, such as the transformation of pulmonary hamartoma into adenocarcinoma, sarcoma or squamous cell carcinoma (15-17). Thus, it is also important to compare and analyze the characteristics of  $^{18}\text{F}$ -FDG PET/CT in benign lung tumors and to evaluate their metabolic activities to choose the proper clinical management. Thus, the present study investigated the characteristics of  $^{18}\text{F}$ -FDG PET/CT in PSH versus pulmonary hamartoma.

## **Materials and methods**

**Patients.** Between November 2015 and August 2017, 12 cases with pathologically defined PSH and 14 cases with pulmonary hamartoma undergoing  $^{18}\text{F}$ -FDG PET/CT examination in the Department of Nuclear Medicine, Shanghai Pulmonary Hospital (Tongji University School of Medicine, Shanghai, China) were enrolled in the present study. The patient characteristics are listed in Table I.

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**<sup>18</sup>F-FDG PET/CT scans and image analysis.** An FDG PET/CT scan was performed on a Biograph 64 system (Siemens Healthineers, Erlangen, Germany) with a 21.6-cm axial field of view. Patients were required to fast for at least 6 h prior to imaging, and serum glucose levels were kept at <7.4 mmol/l. Images were obtained ~60 min after intravenous administration of 3.7-5.6 MBq of FDG per kilogram of body weight. In total, 6 or 7 bed positions from the base of the skull to the mid-thighs were imaged. PET images were acquired for 1.5 min per bed position. CT was performed on the same scanner without contrast administration. The CT scan data were collected under the following conditions: 120 kV, 101 mAs (adjusted by auto mA) and a gantry rotation speed of 0.5 sec. All CT scans were obtained using 5-mm thick axial slices. PET/CT images were analyzed based on CT features and semi-quantitative measurement on the basis of standardized maximum uptake value (SUVmax). SUVmax was calculated as decay-corrected maximum activity concentration in the lesion divided by administered activity divided by body weight in kilograms.

**Pathological examination.** In this study, all 12 patients with PSH and all 14 patients with pulmonary hamartoma underwent resection of the lesion by video-assisted thoracoscopic surgery within 2 weeks of the FDG PET/CT scans. The lung lesions were obtained, and the slides of paraffin-embedded samples were used for common hematoxylin and eosin and immunohistochemical staining. The sections were reviewed by 2 experienced pathologists for the histopathological confirmation of tumor type.

**Statistical analysis.** SPSS 21.0 software for Windows (IBM Corp., Armonk, NY, USA) was used for the statistical analysis (18). Data are expressed as the mean  $\pm$  standard deviation. The association between tumor size and SUVmax was analyzed through Pearson's correlation and linear regression analysis, and the tumor size and SUVmax of two groups were compared using Student's t-test. The 95% confidence level was chosen to determine the significance between groups, with  $P < 0.05$  indicating a statistically significant difference. The cut-off value for the differential diagnosis of PSH and pulmonary hamartoma was obtained through the receiver operating characteristic (ROC) analysis. The areas under the curve, and the sensitivity and specificity of differential diagnosis were calculated.

## Results

As shown in Table I, the mean age of the 12 patients with PSH was  $55 \pm 9$  years. The number of women was greater than that of men, with a ratio of 11:1. The 12 PSHs were all located in the bilateral middle and lower lungs. Among the 12 PSH lesions, 3 lesions exhibited calcification. For the 14 cases of pulmonary hamartoma, the mean age was  $59 \pm 7$  years, and the ratio of women to men was 5:9. These 14 lesions were diffusely located in the bilateral lungs, and the ratio of right-to left-sided lesions was 5:2. Among the 14 pulmonary hamartoma lesions, 4 exhibited calcification.

For the 12 patients with PSH, the mean diameter of all 12 lesions was  $1.9 \pm 0.7$  cm, ranging from 0.6 to 2.9 cm. The mean

Table I. Patient data.

Characteristic	Pulmonary sclerosing hemangioma	Pulmonary hamartoma
Total patients, n	12	14
Mean age (range), years	55 (39-66)	59 (46-72)
Sex, n		
Male	1	9
Female	11	5
Mean size (range), cm	1.9 (0.6-2.9)	1.7 (0.7-3.1)
Lesions, n		
Single	12	14
Multiple	0	0
Localization, n		
RUL	0	2
RML	2	5
RLL	4	3
LUL	0	3
LLL	6	1
Localization, n		
Central	0	0
Peripheral	12	14
Calcification, n		
With	3	4
Without	9	10
Shape, n		
Round	12	14
Irregular	0	0
Margin, n		
Smooth	10	8
Lobular	2	6

RUL, right upper lobe; RML, right middle lobe; RLL, right lower lobe; LUL, left upper lobe; LLL, left lower lobe.

SUVmax was  $2.6 \pm 1.0$ , with a SUVmax ranging from 1.0 to 4.4. There was no significant correlation between the lesion size and SUVmax of PSH ( $P > 0.05$ ,  $r = 0.560$ ,  $r^2 = 0.314$ ) (Fig. 1A). In total, 6 out of 12 PSHs (50%) displayed increased SUVmax values  $> 2.5$ , with SUVmax values of 2.6, 2.6, 2.6, 2.9, 4.4 and 4.4, respectively (Figs. 2 and 3). Fig. 2 presents a case of PSH with an SUVmax of 4.4, and Fig. 3 presents a second case of PSH with an SUVmax of 2.6 and calcification. In addition, no case of PSH with lymph node or lung metastases was observed in the study.

For the 14 cases with pulmonary hamartoma, the mean diameter and SUVmax of all lesions were  $1.7 \pm 0.8$  cm (ranging from 0.7 to 3.1 cm) and  $1.5 \pm 0.6$  (ranging from 0.7 to 2.6), respectively. There was a significant correlation between the lesion size and SUVmax ( $r = 0.625$ ,  $r^2 = 0.391$ ,  $P < 0.05$ ; Fig. 1B). Moreover, only 1 lesion out of 14 pulmonary hamartomas (7%) displayed increased SUVmax values  $> 2.5$ , with a value of 2.6 (Fig. 4).

Furthermore, there was no significant difference between the lesion size of PSH and that of pulmonary hamartoma

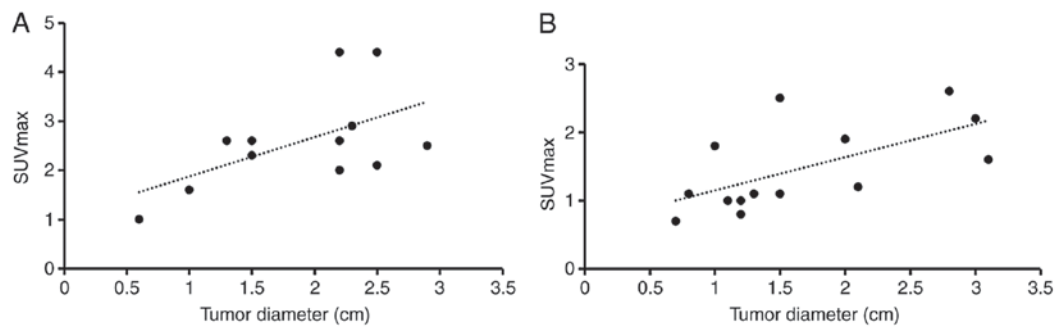


Figure 1. (A) Pearson's correlation and linear regression analysis showed no correlation between the tumor size and the SUVmax of PSH ( $P>0.05$ ,  $r=0.560$ ,  $r^2=0.314$ ). (B) Pearson's correlation and linear regression analysis determined a positive correlation between the tumor size and the SUVmax of pulmonary hamartoma ( $P<0.05$ ,  $r=0.625$ ,  $r^2=0.391$ ). PSH, pulmonary sclerosing hemangioma; SUVmax, maximum standardized uptake value.

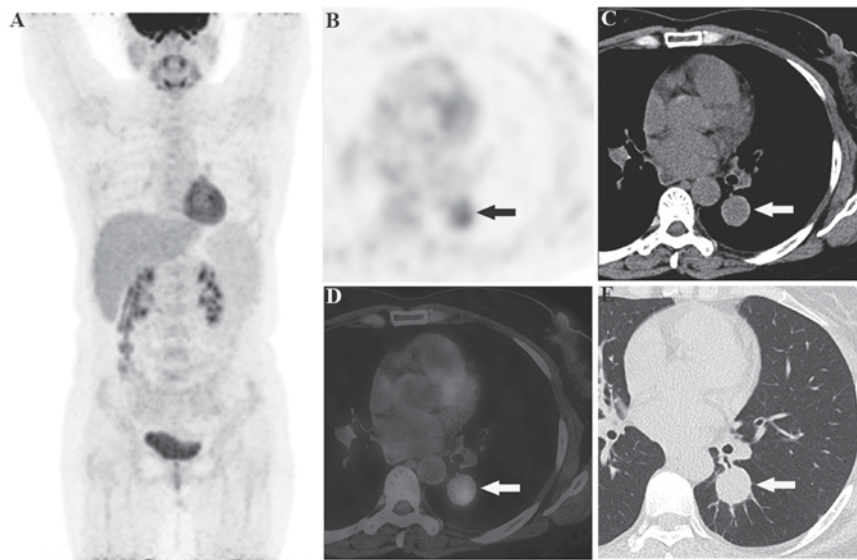


Figure 2. Representative case of a 47-year-old woman who underwent fluorodeoxyglucose PET/CT examination to evaluate a pulmonary nodule of the left lower lobe. (A) The maximum intensity projection image did not show the lesion, which was hidden behind the heart. On the axial images of the chest [(B) PET; (C) mediastinal window of CT; (D) fused PET/CT; (E) lung window of CT], a round lesion (arrow) was present, with a maximum standardized uptake value of 4.4 and a size of  $\sim 2.5 \times 2.4$  cm. The pathology confirmed pulmonary sclerosing hemangioma. PET, positron emission tomography; CT, computed tomography.

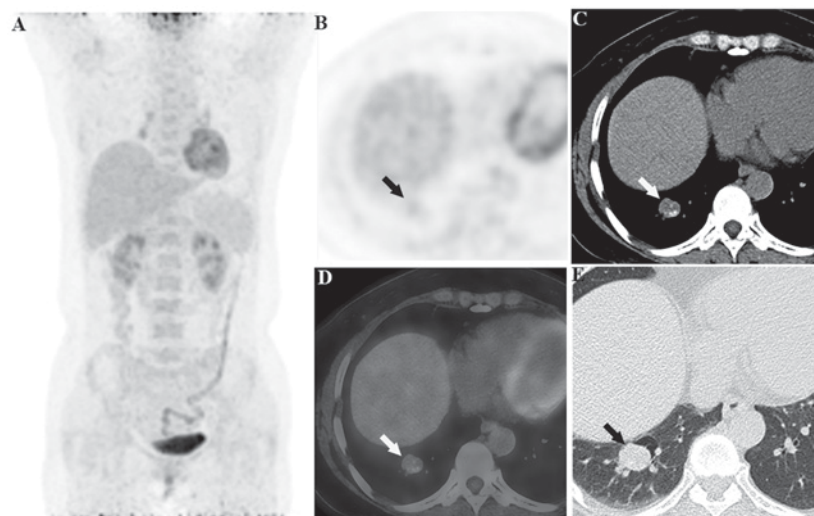


Figure 3. Representative case of a 55-year-old woman who underwent fluorodeoxyglucose PET/CT examination to evaluate a pulmonary nodule of the right lower lobe. (A) The lesion was covered by the liver on the maximum intensity projection image. On the axial images of the chest [(B) PET; (C) mediastinal window of CT; (D) fused PET/CT; (E) lung window of CT], a similar round lesion (arrow) was found. The maximum standardized uptake value was 2.6 and the maximum diameter was 2.2 cm. Finally, the pathology of the nodule confirmed pulmonary sclerosing hemangioma. PET, positron emission tomography; CT, computed tomography.

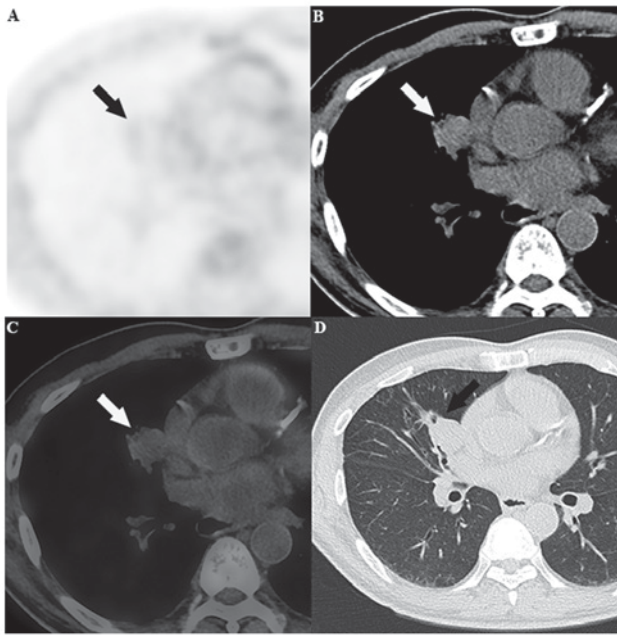


Figure 4. Representative case of a 57-year-old man admitted to hospital due to a cough. A lobular mass of the right middle lung was revealed, which was possibly malignant. The patient underwent fluorodeoxyglucose PET/CT to evaluate the disease extent. The maximum standardized uptake value of the mass (arrow) was 2.2 and the maximum diameter was 3.0 cm on the axial images of the chest [(A) PET; (B) mediastinal window of CT; (C) fused PET/CT]. (D) The lung window of CT revealed obstructive pneumonia at the distal end of the lesion. The pathology confirmed a pulmonary hamartoma. PET, positron emission tomography; CT, computed tomography.

( $P>0.05$ ), but the SUVmax of PSH was significantly higher than that of pulmonary hamartoma ( $P<0.05$ ; Fig. 5). As a cutoff for the differential diagnosis of PSHs versus pulmonary hamartomas, the SUVmax of 1.95 was applied (Fig. 6). The resulting sensitivity and specificity for  $^{18}\text{F}$ -FDG PET/CT to differentiate PSHs from pulmonary hamartomas was 83.3 and 78.6 %, respectively.

## Discussion

PSH has been reported to show various FDG accumulations, with an SUVmax ranging from the background value to 5.3, and the results of the present study were similar to these of previously reported cases (7,19-21). FDG PET/CT scan results are usually interpreted as positive for malignancy when the SUVmax of a lung nodule or mass exceeds 2.5 (22). In the present study, the SUVmax of 50% of the PSHs exceeded 2.5. The high FDG accumulation in PSH should be associated with the tumor size or with potential low-grade malignancy. Lin *et al* (7) observed that larger PSHs tended to show higher FDG uptake on PET/CT scan. Lee *et al* (21) reported that the SUVmax was significantly correlated with tumor size in 8 cases of PSH. However, in the present study of 12 PSH cases, there was no significant correlation between the SUVmax and the tumor size. Moreover, although no case of PSH with lymph node or lung metastases was observed in the present study, the increased FDG in PSH may be mainly associated with the potential low-grade malignant nature.

Uhlén *et al* (8) analyzed 51 patients with pulmonary hamartoma by  $^{18}\text{F}$ -FDG PET/CT and found a median SUVmax

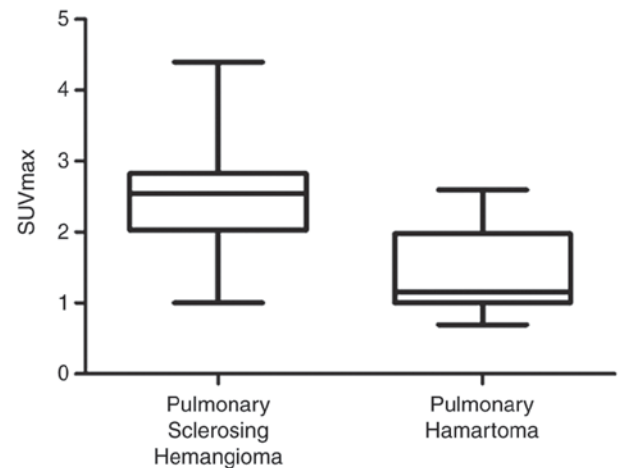


Figure 5. A significant difference was found between the SUVmax of the 12 pulmonary sclerosing hemangiomas and the 14 pulmonary hamartomas ( $P<0.05$ ). SUVmax, maximum standardized uptake value.

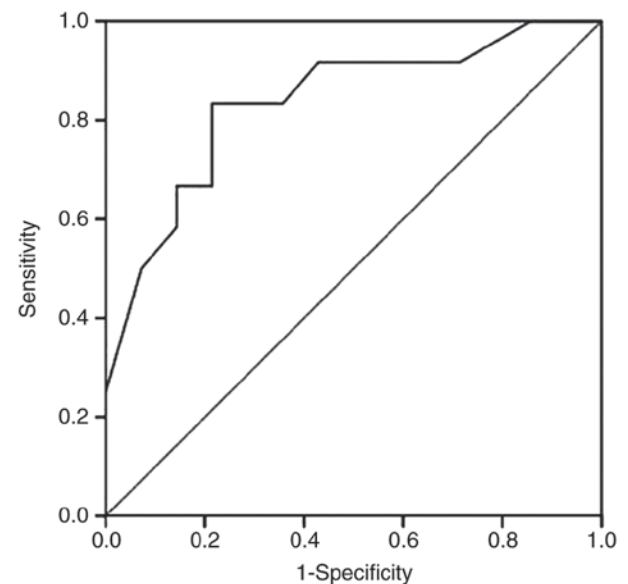


Figure 6. Receiver operating characteristic analysis for determining the cutoff value of the SUVmax in the differential diagnosis of pulmonary sclerosing hemangiomas and pulmonary hamartomas. When the SUVmax of 1.95 was used as the cutoff value, the sensitivity and specificity were 83.3 and 78.6%, respectively. The area under the curve was 0.836 (standard error, 0.082;  $P=0.004$ ; 95% confidence interval, 0.676-0.996).

of 1.4, which was similar to that in the present study. Unlike in PSH, there was a significant correlation between the SUVmax and the tumor size of pulmonary hamartoma in the present study. Moreover, although there was no marked difference between the tumor size, density, shape and margin of the PSHs and pulmonary hamartomas, the study showed significantly higher FDG accumulation in the PSHs than in the pulmonary hamartomas. Chung *et al* (23) suggested that the presence of a hemangiomatous or papillary component in the tumor may lead to increased FDG uptake. Lee *et al* (21) attempted to analyze the mechanism or histological influencing factors of the increased FDG uptake of PSH. However, there were no clear histopathological factors influencing SUVmax in the study, including the tumor component, and glucose transporter



protein-1 (GLUT-1) and GLUT-4 expression. Therefore, influencing factors on the increased FDG uptake of PSH should be further investigated with larger sample sizes.

PSH or pulmonary hamartoma usually presents as a well-defined, peripheral, solitary lung nodule or mass on CT examination, and calcification may occasionally be present. Thus, the majority of PSHs or pulmonary hamartomas could be diagnosed as benign lesions. Due to the poor specificity of the radiological characteristics, few lesions are directly diagnosed as PSH or pulmonary hamartoma even on contrast-enhanced CT examination (1-6). To the best of our knowledge, the present study is the first report on the  $^{18}\text{F}$ -FDG PET/CT characteristics of PSH versus those of pulmonary hamartoma. The present study showed significantly higher FDG accumulation in PSHs than that in pulmonary hamartomas, which may aid the differential diagnosis. The cut-off SUVmax value of 1.95 for the differential diagnosis of PSH and pulmonary hamartoma was obtained through ROC analysis. Among the 12 PSHs, the SUVmax of only 2 lesions was  $<1.95$  (1.0 and 1.6). Meanwhile, the SUVmax of 3 lesions out of the 14 pulmonary hamartomas was  $>1.95$  (2.2, 2.5 and 2.6). When the SUVmax of lung lesions with certain types of benign features, including a round shape, a clear boundary and calcification, exceeds 2.5, it should be distinguished from lung malignancies. In addition, PSH may be low-grade malignancy, since cases of lymph node and lung metastases have been reported. Thus, FDG PET/CT could be useful for the differential diagnosis of low-grade malignancy of PSH, particularly when the SUVmax of PSH exceeds 2.5, or when lymph node and lung metastases are displayed on PET/CT images (9-14), which would be of great assistance in the clinical treatment.

In conclusion, although the morphological features of the two lesion types were not specific, PSH showed significantly higher FDG accumulation than pulmonary hamartoma, and thus, the SUVmax of  $^{18}\text{F}$ -FDG PET/CT may be useful in the differential diagnosis between PSH and pulmonary hamartoma. The main limitation of the present study was the small number of cases, which does not allow for high statistical power. In addition, a correlation analysis between histopathological factors and SUVmax was not performed in the present study, which is another main limitation. Therefore, further studies with a large study population are warranted to confirm the findings of the present study.

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## Availability of data and materials

All data generated or analyzed during this study are included in this published article

## Authors' contributions

HW and LJ conceived and designed the experiments. YH, QT, QZ, YL and XW collected and analyzed the imaging and pathology data. LJ wrote the paper.

## Ethics approval and consent to participate

This retrospective study was approved by the Ethics Committee of Shanghai Pulmonary Hospital (Tongji University School of Medicine, Shanghai, China).

## Consent for publication

The patients in the present study provided written informed consent for the publication of any associated data and accompanying images.

## Competing interests

The authors declare that they have no competing interests.

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