

# A Comparison of $^{68}\text{Ga}$ -DOTATATE and $^{18}\text{F}$ -FDG PET/CT in Pulmonary Neuroendocrine Tumors

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Our purpose was to compare the performance of  $^{68}\text{Ga}$ -1,4,7,10-tetraazacyclododecane-*N,N',N'',N'''*-tetraacetic acid-D-Phe<sup>1</sup>, Tyr<sup>3</sup>-octreotate (DOTATATE), a novel selective somatostatin receptor 2 PET ligand, and  $^{18}\text{F}$ -FDG in the detection of pulmonary neuroendocrine tumors using PET/CT, with correlation of uptake and tumor grade on histology. **Methods:** The imaging findings of the first 18 consecutive patients (8 men and 10 women) with pulmonary neuroendocrine tumors (11 typical carcinoids, 2 atypical carcinoids, 1 large cell neuroendocrine tumor, 1 small cell neuroendocrine carcinoma, 1 non-small cell lung cancer with neuroendocrine differentiation, and 2 cases of diffuse idiopathic pulmonary neuroendocrine cell hyperplasia) who underwent  $^{68}\text{Ga}$ -DOTATATE and  $^{18}\text{F}$ -FDG PET/CT were reviewed. In all cases, the diagnosis was established on histology. **Results:** Of 18 patients, 15 had primary tumors (median size, 2.7 cm; range, 0.5–8 cm) and 3 had recurrent tumors. All typical carcinoids showed high uptake of  $^{68}\text{Ga}$ -DOTATATE (maximum standardized uptake value [ $\text{SUV}_{\text{max}}$ ]  $\geq 8.2$ ), but 4 of 11 showed negative or minimal  $^{18}\text{F}$ -FDG uptake ( $\text{SUV}_{\text{max}} = 1.7$ – $2.9$ ). All tumors of higher grade showed high uptake of  $^{18}\text{F}$ -FDG ( $\text{SUV}_{\text{max}} \geq 11.7$ ), but 3 of 5 showed only minimal accumulation of  $^{68}\text{Ga}$ -DOTATATE ( $\text{SUV}_{\text{max}} = 2.2$ – $2.8$ ). Neither case of diffuse idiopathic pulmonary neuroendocrine cell hyperplasia showed uptake of  $^{68}\text{Ga}$ -DOTATATE or  $^{18}\text{F}$ -FDG. Typical carcinoids showed significantly higher uptake of  $^{68}\text{Ga}$ -DOTATATE and significantly less uptake of  $^{18}\text{F}$ -FDG than did tumors of higher grade ( $P = 0.002$  and  $0.005$ ). There was no instance of false-positive uptake of  $^{68}\text{Ga}$ -DOTATATE, but there were 3 sites of  $^{18}\text{F}$ -FDG uptake secondary to inflammation.  $^{68}\text{Ga}$ -DOTATATE was superior to  $^{18}\text{F}$ -FDG in discriminating endobronchial tumor from distal collapsed lung ( $P = 0.02$ ). **Conclusion:** Typical bronchial carcinoids showed higher and more selective uptake of  $^{68}\text{Ga}$ -DOTATATE than of  $^{18}\text{F}$ -FDG. Atypical carcinoids and higher grades had less  $^{68}\text{Ga}$ -DOTATATE avidity but were  $^{18}\text{F}$ -FDG-avid.

**Key Words:** neuroendocrine; PET/CT;  $^{18}\text{F}$ -FDG;  $^{68}\text{Ga}$ -DOTATATE

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**B**ronchial carcinoids, including typical and atypical carcinoids, comprise 1%–2% of all lung malignancies. They are part of a spectrum of pulmonary neuroendocrine tumors of increasing malignant potential, ranging from low-grade typical carcinoids, through intermediate-grade atypical carcinoids, to more malignant large and small cell neuroendocrine tumors (1–3). In addition, up to 10% of non-small cell lung carcinomas can show neuroendocrine differentiation (1). Whereas  $^{18}\text{F}$ -FDG typically accumulates in small cell carcinomas, indolent tumors such as typical bronchial carcinoids have low glucose turnover, and  $^{18}\text{F}$ -FDG therefore has been thought to be of limited use in the evaluation of these patients (4). Most well-differentiated neuroendocrine tumors express a high density of surface somatostatin receptors, allowing imaging with somatostatin receptor scintigraphy, typically with  $^{111}\text{In}$ -labeled pentetreotide. Novel  $^{68}\text{Ga}$ -DOTA-labeled somatostatin analogs are now finding increasing clinical application (5–8). We have previously compared uptake of  $^{68}\text{Ga}$ -1,4,7,10-tetraazacyclododecane-*N,N',N'',N'''*-tetraacetic acid-D-Phe<sup>1</sup>, Tyr<sup>3</sup>-octreotate (DOTATATE) and  $^{18}\text{F}$ -FDG in neuroendocrine, predominantly gastroenteropancreatic, tumors (6). We now present our initial findings comparing  $^{68}\text{Ga}$ -DOTATATE and  $^{18}\text{F}$ -FDG in pulmonary neuroendocrine tumors.

The purpose of this study was to assess the performance of  $^{68}\text{Ga}$ -DOTATATE, a selective somatostatin receptor subtype 2 tracer, in pulmonary neuroendocrine tumors and to compare the uptake of  $^{68}\text{Ga}$ -DOTATATE and  $^{18}\text{F}$ -FDG using combined PET/CT and correlate uptake of the tracers with tumor grade on histology.

## MATERIALS AND METHODS

### Patients

We retrospectively reviewed the findings for the first 18 consecutive patients (8 men and 10 women; median age, 56 y; range, 33–85 y) with confirmed pulmonary neuroendocrine tumors who underwent  $^{68}\text{Ga}$ -DOTATATE and  $^{18}\text{F}$ -FDG PET/CT at our institution. Pulmonary tumors were classified according to the

method of the World Health Organization (1) into subgroups comprising typical bronchial carcinoid, atypical carcinoid, large cell pulmonary neuroendocrine tumor, small cell neuroendocrine carcinoma of the lung, and non-small cell lung cancer with neuroendocrine differentiation.

Patients were scanned for staging of primary pulmonary neuroendocrine tumor or staging of recurrent tumor. All patients had a diagnosis of pulmonary neuroendocrine tumor confirmed on histologic examination.

The  $^{18}\text{F}$ -FDG and  $^{68}\text{Ga}$ -DOTATATE PET/CT scans were performed within 6 wk of each other (median, 6 d; range, 1–42 d) of study. No patient was treated during the interval between the 2 scans.

All patients gave informed consent, and institutional board ethics approval was received for this retrospective study.

### Combined PET/CT

Images were acquired 1 h after injection of 370 MBq of  $^{18}\text{F}$ -FDG or 45–60 min after injection of 120–200 MBq of  $^{68}\text{Ga}$ -DOTATATE. Imaging was performed using a dedicated GE Discovery ST camera combining a PET unit and a 16-slice CT unit; whole-body examinations (brain to mid thigh) were performed with the patient supine.

The CT exposure factors for all examinations were 120 kVp and 80 mA in 0.8 s. Maintaining patient position, we performed a whole-body PET emission scan covering an area identical to that covered by CT. PET scans were acquired at a rate of 4 min per bed position, and PET images were reconstructed using CT for attenuation correction. The  $^{18}\text{F}$ -FDG PET acquisition was performed in 2 dimensions with a 3-slice overlap between consecutive bed positions. Transaxial  $^{18}\text{F}$ -FDG PET data were reconstructed using ordered-subsets expectation maximization with 2 iterations and 21 subsets. The  $^{68}\text{Ga}$ -DOTATATE PET acquisition was performed in 3 dimensions with a 5-slice overlap between consecutive bed positions.  $^{68}\text{Ga}$ -DOTATATE PET images were reconstructed using an ordered-subsets expectation maximization algorithm with 3 iterations and 25 subsets. The CT data for  $^{68}\text{Ga}$ -DOTATATE and  $^{18}\text{F}$ -FDG PET/CT were reconstructed to axial slices 3.75 mm thick with a soft-tissue reconstruction algorithm and 2.5 mm thick with a lung reconstruction algorithm.

### Image Review

The  $^{68}\text{Ga}$ -DOTATATE and  $^{18}\text{F}$ -FDG PET/CT studies were reviewed for areas of abnormally increased tracer uptake by an experienced nuclear medicine physician and by a physician certified in both radiology and nuclear medicine. The pattern of tracer uptake and a semiquantitative parameter (maximum standardized uptake value [ $\text{SUV}_{\text{max}}$ ]) were documented in all lesions and in atelectatic lung distal to endobronchial tumor. Tracer uptake was correlated with the anatomic extent of tumor on surgical resection to differentiate uptake in tumor from uptake in distal collapsed lung. In those patients with multiple tumor lesions, the mean  $\text{SUV}_{\text{max}}$  was calculated for all lesions. (A positive scan was defined as significant accumulation of tracer based on visual assessment by the 2 observers). The unenhanced CT studies from the PET/CT acquisition were also used to document lesion characteristics. Image findings for the 2 tracers were compared with each other and with histologic findings. The diagnosis of tumor was established on the basis of histology in all cases.

### Statistical Analysis

The Mann–Whitney test was used to calculate differences in uptake between typical carcinoids and tumors of higher grade for both  $^{68}\text{Ga}$ -DOTATATE and  $^{18}\text{F}$ -FDG. The Mann–Whitney test was also used to compare differences in the ratio of tumor uptake to atelectatic lung uptake between  $^{68}\text{Ga}$ -DOTATATE and  $^{18}\text{F}$ -FDG. A *P* value of less than 0.05 was taken as significant for both tests.

## RESULTS

### Tumor Overview (Table 1)

Eleven patients had typical bronchial carcinoids, and 5 had higher-grade pulmonary neuroendocrine tumors [2 atypical carcinoids, 1 large cell neuroendocrine tumor, 1 non-small cell lung carcinoma (adenocarcinoma) with neuroendocrine differentiation, and 1 small cell neuroendocrine carcinoma]. Two patients had diffuse idiopathic pulmonary neuroendocrine cell hyperplasia, with multiple carcinoid tumorlets ( $\leq 5$  mm in diameter) in one and multiple tumorlets and carcinoid tumors ( $\leq 1.3$  cm) in the other.

Fifteen patients had primary tumors. Primary tumors presented as pulmonary nodules or masses, with a median size of 2.7 cm (range, 0.5–8 cm). One primary tumor showed spread along both the bronchial tree and the surrounding parenchyma (“iceberg tumor,” Fig. 1). Three patients with primary tumors (1 large cell, 1 adenocarcinoma with neuroendocrine differentiation, and 1 small cell neuroendocrine carcinoma) had metastatic spread to the lung (1 patient), the mediastinal nodes (2 patients), the skeleton (1 patient), or the liver (2 patients). The diagnosis of metastatic disease was made by findings of progressive disease on imaging follow-up ( $\geq 1$  y) and histology (2 patients). Nine patients with primary tumors (all typical carcinoids) presented with endobronchial tumors. Of these 9 patients, 8 had collapsed lung distal to the tumor.

Three patients had recurrent pulmonary neuroendocrine tumors after resection of the primary tumor. These patients presented with tumor metastases in the skeleton (2 patients), with pulmonary nodules or masses (2 patients), with nodal metastases (2 patients), or with a chest wall metastasis (1 patient).

No tumors (primary or recurrent) showed features of ectopic hormonal secretion (e.g., carcinoid or Cushing syndrome).

### Comparison of Uptake of $^{68}\text{Ga}$ -DOTATATE and $^{18}\text{F}$ -FDG with Tumor Histology

The median  $\text{SUV}_{\text{max}}$  of  $^{68}\text{Ga}$ -DOTATATE for all tumors was 15 (range, 1–118) (Table 1). All typical carcinoids showed high  $^{68}\text{Ga}$ -DOTATATE uptake ( $\text{SUV}_{\text{max}} \geq 8.2$ , Fig. 2). Three of the 5 tumors of a higher grade than typical carcinoids had only minimal  $^{68}\text{Ga}$ -DOTATATE accumulation ( $\text{SUV}_{\text{max}} = 2.2$ –2.8). Typical carcinoids showed significantly higher  $^{68}\text{Ga}$ -DOTATATE uptake than did

**TABLE 1.** Summary of Tumor Characteristics and Scan Findings

Patient no.	Tumor type	<sup>68</sup> Ga-DOTATATE uptake (SUV <sub>max</sub> )	<sup>18</sup> F-FDG uptake (SUV <sub>max</sub> )	Location of primary tumor	Size of primary tumor (cm)	Tumor site	Histology
1	Primary	33	7.2	Central	2.3	Primary	Typical carcinoid
2	Primary	8.2	6.7	Central	1.5	Primary	Typical carcinoid
3	Primary	44.9	2.3	Central	3.2	Primary	Typical carcinoid
4	Primary	18	2.9	Central	2.8	Primary	Typical carcinoid
5	Primary	29.4	2.9	Central	2.1	Primary	Typical carcinoid
6	Primary	45	3.4	Central	5.5	Primary	Typical carcinoid
7	Primary	118	16	Central	3.2	Primary	Typical carcinoid
8	Primary	12	4.9	Peripheral	2.6	Primary	Typical carcinoid
9	Primary	2.8	20.5	Central	8	Primary, mediastinal node	Small cell neuroendocrine carcinoma
10	Primary	42.7	6.3	Central	5.8	Primary	Typical carcinoid
11	Primary	65	6	Central	1.5	Primary	Typical carcinoid
12	Recurrent metastatic	24	1.7	NA	—	Skeletal	Typical carcinoid
13	Primary	1.0	1.1	Multiple peripheral	0.5	Primary (multiple nodules)	Carcinoid tumorlets*
14	Primary	2.2	18.5	Peripheral	4	Lung, mediastinal node, liver	Large cell pulmonary neuroendocrine tumor
15	Primary	1.5	1.5	Central and peripheral	≤1.3	Lung	Multiple carcinoid tumorlets and tumors*
16	Recurrent metastatic	5.1	11.7	NA	—	Lung, chest wall, extrathoracic node	Atypical carcinoid
17	Recurrent metastatic	4.7	14.5	NA	—	Lung, mediastinal node, skeletal	Atypical carcinoid
18	Primary	2.7	16	Central	2.8	Primary, liver, skeletal	Adenocarcinoma with neuroendocrine differentiation

\*Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia.  
NA = not applicable.

tumors of higher grade (median SUV<sub>max</sub> = 33 [range, 8.2–118] vs. 2.8 [range, 2.2–5.1],  $P = 0.002$  (Table 2)).

The median SUV<sub>max</sub> of <sup>18</sup>F-FDG for all tumors was 6.1 (range, 1.1–20.5). Four of the 11 patients with typical carcinoids showed no <sup>18</sup>F-FDG uptake or only mild uptake (SUV<sub>max</sub> = 1.7, 2.3, 2.9, and 2.9, Fig. 2). All tumors of higher grade than typical carcinoids showed high <sup>18</sup>F-FDG uptake (SUV<sub>max</sub> ≥ 11.7). Typical carcinoids showed significantly less uptake of <sup>18</sup>F-FDG than did tumors of higher grade (median SUV<sub>max</sub> = 4.9 [range, 1.7–16] vs. 16 [range, 11.7–20.5],  $P = 0.005$ ). Neither patient with diffuse idiopathic pulmonary neuroendocrine cell hyperplasia showed uptake of <sup>68</sup>Ga-DOTATATE (SUV<sub>max</sub> = 1.0 and 1.5) or <sup>18</sup>F-FDG (SUV<sub>max</sub> = 1.1 and 1.5).

No false-positive uptake of <sup>68</sup>Ga-DOTATATE was seen, but there were 3 sites of false-positive uptake of <sup>18</sup>F-FDG in hilar nodes (1 patient) and in atelectatic lung distal to tumor (2 patients).

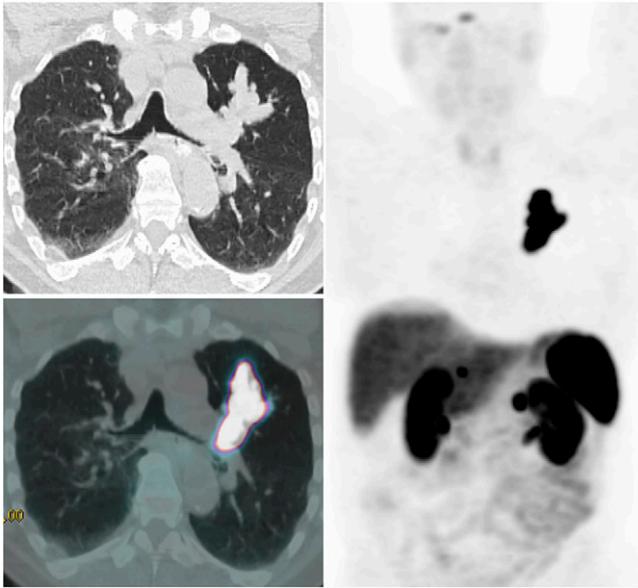
There was mild <sup>68</sup>Ga-DOTATATE uptake (SUV<sub>max</sub> = 1.2–3.3) and more intense <sup>18</sup>F-FDG uptake (SUV<sub>max</sub> = 0.7–18.2) in collapsed lung distal to endobronchial tumor (Table 3; Fig. 3). The ratio of tumor uptake to atelectatic

lung uptake in endobronchial carcinoid tumors was significantly higher for <sup>68</sup>Ga-DOTATATE than for <sup>18</sup>F-FDG (Table 3,  $P = 0.02$ ).

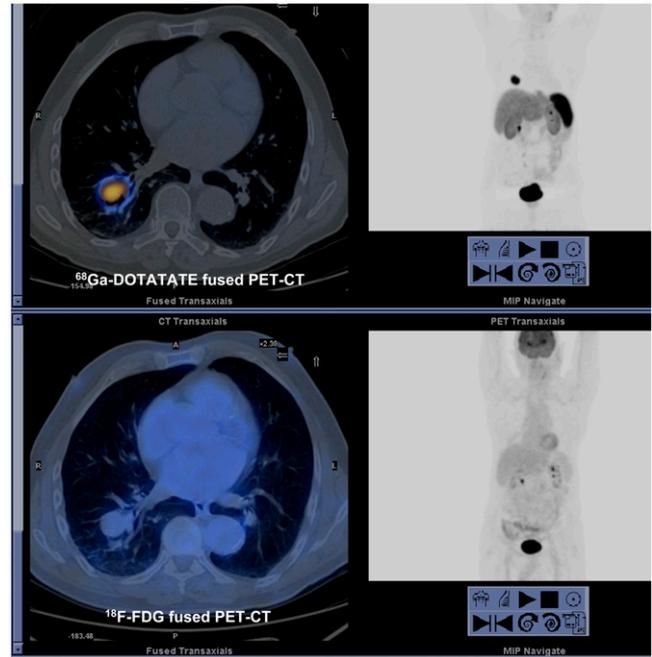
## DISCUSSION

This paper describes the first (to our knowledge) comparison of the novel PET somatostatin receptor 2 ligand <sup>68</sup>Ga-DOTATATE and <sup>18</sup>F-FDG in pulmonary neuroendocrine tumors. <sup>68</sup>Ga-DOTATATE was superior to <sup>18</sup>F-FDG in typical histologically well-differentiated bronchial carcinoids and was able to correctly delineate endobronchial tumor from adjacent atelectasis.

A good correlation was observed between grade of pulmonary neuroendocrine tumor and <sup>68</sup>Ga-DOTATATE and <sup>18</sup>F-FDG uptake; we have previously reported similar results in patients with gastroenteropancreatic neuroendocrine tumors (6). All typical carcinoids showed high uptake of <sup>68</sup>Ga-DOTATATE (SUV<sub>max</sub> ≥ 8.2). In contrast, <sup>18</sup>F-FDG uptake was variable; although most typical carcinoids showed uptake of <sup>18</sup>F-FDG, in half the tracer uptake was low, with SUV<sub>max</sub> no more than 3.4. Our study supports



**FIGURE 1.** Coronal oblique CT (top), fused  $^{68}\text{Ga}$ -DOTA-TATE PET/CT (bottom), and maximum-intensity-projection (right) images of 79-y-old man (patient 3) with large, 5-cm, endobronchial carcinoid tumor in left-upper-lobe bronchus. Tumor extension is centered on bronchovascular bundle, with invasion of adjacent lung parenchyma.



**FIGURE 2.** Fused PET/CT (left) and maximum-intensity-projection (right) images of 85-y-old man (patient 4) with typical bronchial carcinoid in right lower lobe. Tumor shows intense  $^{68}\text{Ga}$ -DOTATATE uptake but has minimal avidity for  $^{18}\text{F}$ -FDG.

previous evidence that the role of  $^{18}\text{F}$ -FDG PET/CT in the evaluation of typical bronchial carcinoids is limited by their indolent nature and slow metabolism. Erasmus et al. (4) reported low  $^{18}\text{F}$ -FDG uptake ( $\text{SUV}_{\text{max}} < 2.5$ ) in 5 of 6 typical bronchial carcinoids. More recent studies have found a higher sensitivity of 50% (6/12) (9) and 73% (8/11) (10) for detection of typical bronchial carcinoids. Tumors of a higher grade than typical bronchial carcinoids had high  $^{18}\text{F}$ -FDG uptake ( $\text{SUV}_{\text{max}} \geq 11.7$ ), but more than half were negative for  $^{68}\text{Ga}$ -DOTATATE accumulation or showed only minimal uptake ( $\text{SUV}_{\text{max}} = 2.2\text{--}2.8$ ), although the cases were few. This finding is in keeping with previous data from Chong et al., who reported higher  $^{18}\text{F}$ -FDG uptake in large cell and small cell neuroendocrine carcinomas (11). In vitro studies have shown that somatostatin receptor–negative lung carcinoids usually belong to the less differentiated atypical variety of neoplasms (12). The correlation of  $^{18}\text{F}$ -FDG and  $^{68}\text{Ga}$ -DOTATATE uptake with tumor grade identifies a potential use for assessing pulmonary neuroendocrine tumors. It is possible that avidity of  $^{18}\text{F}$ -FDG or  $^{68}\text{Ga}$ -DOTATATE could be used to help identify, at initial staging and also during follow-up and subsequent therapy, aggressive tumors containing sites of possible dedifferentiation.

Most pulmonary carcinoids are indolent typical carcinoids with metastases in only 15% and with 5-y survival of over 90% (2). Typical carcinoids arise 3–4 times more frequently than atypical carcinoids, which tend to occur in older patients, are more commonly larger, and more often arise peripherally. They metastasize in 30%–50% of cases and

have a 5-y survival rate of 40%–60% (13). Patients with pulmonary neuroendocrine tumor often present with recurrent pneumonia, cough, hemoptysis, or chest pain. Our patients presented with similar symptoms but with no clinical evidence of carcinoid syndrome or ectopic adrenocorticotrophic hormone production, which are rare manifestations of these tumors, occurring in less than 5% of cases (2). Typical bronchial carcinoids have a predilection for the central airways and often may present as endobronchial tumors (14). Endobronchial tumors can be treated with conservative surgical techniques, for example, sleeve resection, wedge resection, or segmental resection sparing as much of the normal lung tissue as possible. In a significant proportion, there is adjacent extrabronchial spread (iceberg tumor), which necessitates lobectomy (2). In our series, an iceberg tumor

**TABLE 2.** Tumor Uptake of  $^{68}\text{Ga}$ -DOTATATE and  $^{18}\text{F}$ -FDG

Tumor type	$^{68}\text{Ga}$ -DOTATATE uptake ( $\text{SUV}_{\text{max}}$ )	$^{18}\text{F}$ -FDG uptake ( $\text{SUV}_{\text{max}}$ )
Low-grade tumors (typical carcinoids)	33 (8.2–118)	4.9 (1.7–16)
Atypical and higher-grade tumors	3.5 (2.2–5.1)	16 (11.7–20)

Values are medians and ranges.

**TABLE 3.** Uptake of  $^{68}\text{Ga}$ -DOTATATE and  $^{18}\text{F}$ -FDG in Tumor and Atelectatic Lung

Histology	Uptake in collapsed lung ( $\text{SUV}_{\text{max}}$ )		Ratio of tumor uptake to collapsed distal lung uptake	
	$^{68}\text{Ga}$ -DOTATATE	$^{18}\text{F}$ -FDG	$^{68}\text{Ga}$ -DOTATATE	$^{18}\text{F}$ -FDG
Typical bronchial	1.2	0.7	27.5	10.3
Typical bronchial	3.3	18.2	2.5	3.7
Typical bronchial	1.2	2.9	15	1.0
Typical bronchial	2.8	11.2	10.5	0.26
Typical bronchial	1.8	4	25	0.85
Typical bronchial	1.3	3	91	5.3
Typical bronchial	1.9	2.4	22.5	2.6
Typical bronchial	1.3	2.9	50	2.2

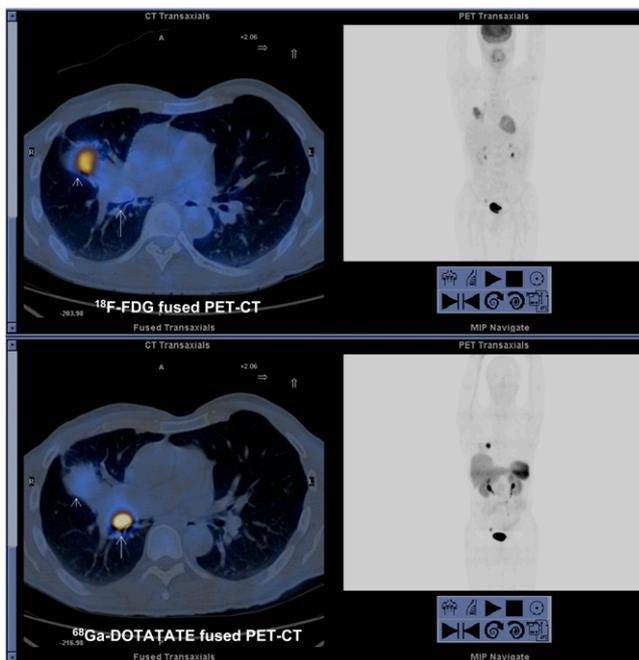
and its endo- and extrabronchial spread were clearly demonstrated by  $^{68}\text{Ga}$ -DOTATATE but not by  $^{18}\text{F}$ -FDG (Fig. 1).

On the basis of the low-level but definite  $^{18}\text{F}$ -FDG avidity of most typical bronchial carcinoid tumors, some investigators have recommended  $^{18}\text{F}$ -FDG PET as a useful technique for preoperative evaluation (9,10). However, caution should be exercised in this regard. We have shown high accumulation of  $^{18}\text{F}$ -FDG in collapsed lung distal to endobronchial carcinoids secondary to obstructive pneumonia (Fig. 3; Table 3)—a finding that, to our knowledge, has not previously been described. This finding is in contrast to the ability of  $^{18}\text{F}$ -FDG PET/CT to show high

uptake in tumor over adjacent atelectasis in non-small cell lung carcinoma (15,16). Carcinoid tumor may be outlined as a relatively cold region of  $^{18}\text{F}$ -FDG uptake, or if tumor and inflammatory uptake are comparable, delineation of tumor boundaries may be difficult with  $^{18}\text{F}$ -FDG. Furthermore,  $^{18}\text{F}$ -FDG uptake could be incorrectly ascribed to tumor within collapsed lung, hilar nodes, and mediastinal nodes. At present, contrast-enhanced CT with multiplanar reconstruction and bronchoscopy is used for locoregional tumor staging.  $^{18}\text{F}$ -FDG PET/CT has little role, but  $^{68}\text{Ga}$ -DOTATATE PET/CT—because of high selective uptake in typical carcinoids—may also be useful in some cases, such as when discrimination between tumor and atelectasis is difficult on contrast-enhanced CT.

We also describe the use of PET/CT in diffuse idiopathic pulmonary neuroendocrine cell hyperplasia, which is thought to represent a rare precursor for typical and atypical carcinoids and is characterized by a diffuse proliferation of pulmonary neuroendocrine cells that can manifest as multiple tumorlets ( $\leq 5$  mm in diameter) (17). If nodules are 6 mm or larger, they are named carcinoid tumors. Neither of the 2 cases in our cohort showed accumulation of  $^{68}\text{Ga}$ -DOTATATE or  $^{18}\text{F}$ -FDG, possibly because of small lesion size or low somatostatin receptor expression. Because of its intrinsic partial-volume limitation, PET/CT is unlikely to be of clinical benefit in these patients.

The superior resolution and anatomic localization of  $^{68}\text{Ga}$ -DOTATATE PET with integrated CT fusion offer advantages over conventional imaging with  $^{111}\text{In}$ -pentetate for diagnosis and therapy planning. Furthermore, the affinity profile of  $^{68}\text{Ga}$ -DOTATATE shows distinctly superior preclinical, pharmacologic performance to the  $^{111}\text{In}$ -labeled peptides, especially in somatostatin receptor 2-expressing cells (18). In higher-grade or metastatic bronchial carcinoids, uptake of  $^{68}\text{Ga}$ -DOTATATE is likely to be less intense and less extensive. In these patients, however,  $^{68}\text{Ga}$ -DOTATATE imaging may still have clinical value because of the potential for targeted radionuclide therapy, such as with  $^{177}\text{Lu}$ -DOTATATE (19,20). To assess somatostatin receptor expression against overall tumor burden, further imaging with  $^{18}\text{F}$ -FDG PET/CT or contrast-enhanced CT may be valuable.



**FIGURE 3.** Fused PET/CT (left) and maximum-intensity-projection (right) images of 60-y-old man (patient 5) with typical endobronchial carcinoid (arrows) in middle-lobe bronchus. Lung is collapsed distal to tumor (arrowheads) and showed intense obstructive pneumonia on histology.  $^{68}\text{Ga}$ -DOTATATE shows highly selective uptake in tumor, whereas  $^{18}\text{F}$ -FDG shows mild uptake in tumor and much higher uptake in collapsed lung.

The limitations of our study include the relatively small sample size, the retrospective nature of the study, and lack of Ki67 index in all patients. In this study, only 20% of patients had the Ki67 index performed with tumor histology. The Ki67 index is one of the most useful discriminators of tumor grade and is a prognostic marker in neuroendocrine tumors (21,22). A specific comparison of uptake with Ki67 index in pulmonary NET would have been useful; we have previously shown a relationship between  $^{18}\text{F}$ -FDG and  $^{68}\text{Ga}$ -DOTATATE uptake and tumor proliferation assessed with the Ki67 index in gastroenteropancreatic neuroendocrine tumors (6), but Ki67 staining was not performed in all patients and therefore could not be assessed. None of our tumors had active hormonal secretion, and therefore the results of the study cannot necessarily be extrapolated to these clinical scenarios.

## CONCLUSION

High and selective uptake of  $^{68}\text{Ga}$ -DOTATATE, a somatostatin receptor 2 PET radioligand, is seen in typical bronchial carcinoid tumors. High-grade tumors had lower uptake of  $^{68}\text{Ga}$ -DOTATATE but were  $^{18}\text{F}$ -FDG-avid.  $^{18}\text{F}$ -FDG was poor at discriminating tumor from distal atelectasis.  $^{68}\text{Ga}$ -DOTATATE, with integrated PET/CT, can be useful for presurgical planning in cases of primary bronchial carcinoid and for staging of recurrent pulmonary neuroendocrine tumors.

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