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Review Article

The value of ^{68}Ga-DOTATATE PET/CT in diagnosis and management of neuroendocrine tumors compared to current FDA approved imaging modalities: a review of literature

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Abstract: Neuroendocrine tumors (NETs) are rare group of neoplasms arising from nervous and endocrine systems. Somatostatin analogue imaging is a functional imaging modality of choice for evaluating the NETs. Recent availability of positron emitting radioisotope labeled somatostatin analogues to image neuroendocrine cancers, has raised the interests to use this new imaging modality in management of patients with NETs. ^{68}Ga-DOTATATE PET/CT has demonstrated superiority in lesion detection compared to Octreoscan, MIBG scintigraphy and MRI. In this article, we reviewed the published studies evaluating the role of ^{68}Ga-DOTATATE PET in diagnosis and management of patients with neuroendocrine tumors and comparing it to current FDA approved imaging modalities including Octreoscan, MIBG scintigraphy, ^{18}F FDG PET/CT, CT and MRI.

Keywords: Gallium 68, neuroendocrine tumors, DOTATATE, positron emission tomography, hybrid imaging

Introduction

Neuroendocrine tumors (NETs) are a rare group of neoplasms with an incidence of about 35 cases per 100,000 people in the United States. The defined characteristic of NETs is the expression of somatostatin receptors (SST) [1]. This unique feature has enabled the field of nuclear medicine and molecular imaging to image these tumors with radiolabelled somatostatin analogues agent [2]. Octreotide, a long-acting somatostatin analogue, was initially used in 1989 and since then it evolved as an important agent in the initial evaluation and management of NETs using molecular imaging techniques [3]. However, gamma imaging using ^{111}In-octreotide has several limiting factors which decreased the image quality and overall efficiency of the test. These include low image quality of indium 111 isotope, increased physiological uptake which restricts detection of small lesions, prolonged imaging protocol and relatively high radiation dose to the patients [4, 5].

Radiolabelled meta-iodobenzylguanidine (MIBG) with liodide 123 or 131 has been used in a subgroup of neuroendocrine cancers including pheochromocytoma and paraganglioma [6]. MIBG imaging has been used as a standard functional imaging for initial evaluation and management of these types of tumors. However, the spatial resolution of MIBG imaging is low and has limitations similar to Octreoscan®. Contrast-enhanced MRI is also used to evaluate neuroendocrine tumors due to its ability to provide high quality images of the abdomen [7] but their specificity is poor, especially for phaeochromocytomas [8].

With recent availability of the PET imaging technique, somatostatin analogues have been labeled with positron emitting isotopes, including Gallium-68, to image somatostatin receptor expressing tumors [9]. It has been demonstrated that ^{68}Ga-DOTATATE PET scan can dramatically improve the spatial resolution and lesion detectability compared to Octreoscan® or

Table 1. Demographic data

Author	Journal	Year	No Patients	Tumor	Lesions	Reference
Goel et al	IJNM	2014	30	All NET	Mets	[26]
Armbruster et al	JIR	2014	42	All NET	Liver Mets	[27]
Haug et al	Radiology	2013	63	All NET (Excluded MTC)	Mets	[19]
Schmid et al	EJNMMI	2013	18	Pancreatic NET	Panc lesions+mets	[25]
Haug et al	JNM	2012	104	All NET	Primary lesions+mets	[18]
Maurice et al	EJNMMI	2012	15	PCC, PGL	Primary lesions+mets	[23]
Hofman et al	JMIRO	2012	59	NET (GEP, Bronc, PCC, PGL)	Primary lesions+mets	[12]
Łapińska et al	NMRCEE	2011	97	NET (GEP, MCT)	Primary lesions+mets	[21]
Naji et al	MIAB Aug	2010	12	PCC, PGL	Primary lesions+mets	[24]
Srirajaskanthan et al	JNM June	2010	51	All NET	Primary lesions+mets	[20]
Conry et al	EJNMMI	2010	18	MTC	Primary lesions+mets	[28]
Kayani et al	JNM	2009	18	All NET	Primary lesions+mets	[30]
Kayani et al	Cancer	2008	38	All NET	Primary lesions+mets	[28]
Win et al	NMC	2007	5	PCC	Mets	[22]

NET: Neuroendocrine Tumor, MTC: Medullary Thyroid Cancer, PCC: Pheochromocytoma, PGL: Paraganglioma, GEP: Gastroenteropancreatic, Bronc: Bronchial.

Table 2. ^{68}Ga-DOTATATE sensitivity and specificity compared to pathology as a gold standard

Author	^{68}Ga-DOTATATE	Pathology	Reference
Haug et al	Sensitivity 90% (GEP 94%)	(gold standard)	[17]
	Specificity 82% (GEP 89%)		
Haug et al	Sensitivity 81%	(gold standard)	[18]
	Specificity 90%		

MIBG scintigraphy [9, 10]. In terms of convenience ^{68}Ga-DOTATATE represents a major advantage for patients as it can be completed in less than 2 hours versus 2 days for Octreoscan or MIBG imaging. ^{68}Ga-DOTATATE also involves lower radiation exposure [11]. However, the superiority of ^{68}Ga-DOTATATE PET imaging is due to the added diagnostic information and also quantification capability in comparison with Octreoscan® or MIBG imaging. ^{68}Ga-DOTATATE has also been proven to have high impact on management of the neuroendocrine cancer patients indicating an important role in clinical practice of somatostatin-avid malignancies [12].

The purpose of this article is to systematically review all published data on the role of ^{68}Ga-DOTATATE PET in diagnostic and management of patients with neuroendocrine cancer and compare it to current FDA approved imaging modalities including Octreoscan®, MIBG scintigraphy, ^{18}F FDG PET/CT, CT and MRI.

Literature review methodology

A comprehensive electronic literature search of the Pubmed and ovid medline databases was performed to find published articles on the diagnostic and management value of ^{68}Ga-DOTATATE PET/CT in NETs patients. We searched using words "Ga 68 or gallium 68" and DOTATATE or DOTA TATE or DOTA-TATE or DOTA octreotide. We defined our search time with no beginning date but ending 15 February 2014. Only English language journals were searched in the database. We included all the articles investigating the diagnostic and management role of ^{68}Ga-DOTATATE PET in patients with NETs comparing to Octreoscan, MIBG scintigraphy or MRI. We excluded the articles that were: review articles, case reports, editorial, letters, author reply, comments, duplicate data, using other radiopharmaceuticals such as ^{68}Ga-DOTATOC studies and articles that were not related to neuroendocrine tumors. The search was performed by three researchers (AM, ST and ED) and all the retrieved abstracts were reviewed carefully and eventually selected according to the inclusion and exclusion criteria described above. All the researchers then reviewed the full papers and their eligibility for inclusion was determined in the consensus meeting.

Basic information from these studies were extracted including authors, type of NETs,

Table 3. Comparing the ^{68}Ga-DOTATATE to Octreoscan

Author	^{68}Ga-DOTATATE	Octreoscan	Pathology confirmed	Reference
Hofman et al	Sensitivity 88%	Sensitivity n/a	41/59 patients (11 suspicious, 4 confirmed with imaging)	[12]
	Specificity 80%	Specificity n/a		
Srirajaskanthan et al	Sensitivity 87.2%	Sensitivity n/a	Yes all 51 patients	[19]
	Specificity 100%	Specificity 98%		
Łapińska et al	Sensitivity n/a	Sensitivity n/a	88/97 patients (9 Suspicious)	[20]
	Specificity n/a	Specificity n/a		

Table 4. Comparing the ^{68}Ga-DOTATATE to MIBG scintigraphy

Author	^{68}Ga-DOTATATE	MIBG	Pathology confirmed	Reference
Win et al	Sensitivity 100%	Sensitivity 60%	No	[21]
	Specificity 100%	Specificity n/a		
Maurice et al	Sensitivity 80%	n/a (used as a gold standard)	Yes all 15 patients	[22]
	Specificity n/a			
Naji et al	Sensitivity 83%	Sensitivity 41.6%	8/12 patients (4 confirmed with imaging)	[23]
	Specificity n/a	Specificity n/a		

country, patient information, study design, reference standard. The value of sensitivity and specificity ^{68}Ga-DOTATATE PET in the diagnosis of NETs were recorded.

As only few studies, following the above mentioned criteria, were found ineach category comparing the ^{68}Ga-DOTATATE PET/CT to Octreoscan, MIBG scintigraphy or MRI, no statistical analysis was performed. The sensitivity and specificity of ^{68}Ga-DOTATATE PET/CT were obtained from individual studies and compared to Octreoscan, MIBG scintigraphy and CT or MRI.

Results

Literature search

The comprehensive literature search showed 73 published papers. Upon review, 59 papers were excluded as they were reviews, letters, or editorials, or because they were not within the field of interest of this review. Finally 14 papers were selected and retrieved in full text version. A total of 570 patients with NETs [17-26], satisfying inclusion and exclusion criteria were included in this review. The characteristics of the included studies are presented in **Table 1**.

Diagnostic performance

The summary data of ^{68}Ga-DOTATATE PET/CT is presented in **Table 1**. The sensitivity of the ^{68}Ga-DOTATATE PET/CT in the diagnosis of primary or metastatic lesions in NETs is specified in **Tables 2**-**4** ranging 80%-100%. The specificity of the ^{68}Ga-DOTATATE PET/CT in the diagnosis of primary or metastatic lesions in NETs compared to gold standard pathology is demonstrated in **Table 2** ranging 82%-90%.

^{68}Ga-DOTATATE PET/CT versus Octreoscan

3 studies compared the ^{68}Ga-DOTATATE PET/CT to Octreoscan (**Table 3**). The total number of patients in these studies was 207. The sensitivity of the ^{68}Ga-DOTATATE PET/CT ranged from 83%-88% and its specificity ranged from 80%-100%. The specificity of the Octreoscan mentioned only in one study which was 98%. No sensitivity of Octreoscan was reported in these 3 studies.

^{68}Ga-DOTATATE PET/CT versus Octreoscan: change in clinical management

Two of 3 studies mentioned above reported that the additional information provided by ^{68}Ga-DOTATATE PET resulted in change in clinical management in 70.6%-81% of patients with neuroendocrine cancers.

^{68}Ga-DOTATATE PET/CT versus MIBG scintigraphy

There were 3 studies comparing the ^{68}Ga-DOTATATE PET/CT to MIBG scintigraphy (**Table**

Table 5. Comparing the ^{68}Ga-DOTATATE to MRI or CT

Author	^{68}Ga-DOTATATE	MRI or CT	Pathology confirmed	Reference
Schmid et al	Sensitivity 100%	Sensitivity 63.1%	Yes all 18 patients	[24]
	Specificity 100%	Specificity n/a		
Goel et al	Sensitivity n/a	Sensitivity n/a	No	[25]
	Specificity n/a	Specificity n/a		
Armbruster et al	Sensitivity 92.6%	Sensitivity n/a	No	[26]
	Specificity 93.8%	Specificity n/a		

Table 6. Comparing the ^{68}Ga-DOTATATE to ^{18}F-FDG PET/CT

Author	^{68}Ga-DOTATATE	^{18}F-FDG PET/CT	Pathology confirmed	Reference
Kayani et al	Sensitivity 82%	Sensitivity 66%	Not all patients	[27]
	Specificity n/a	Specificity n/a		
Kayani et al	Sensitivity 100%	Sensitivity 54.4%	Not all patients	[28]
	Specificity n/a	Specificity n/a		
Conry et al	Sensitivity 72.2%	Sensitivity 77.8%	Not all patients	[29]
	Specificity n/a	Specificity n/a		

4). The total number of patients in these studies was 32. The sensitivity of the ^{68}Ga-DOTATATE PET/CT ranged from 80%-100% and its specificity only reported in one study which was 100%.

The sensitivity of the MIBG scintigraphy ranged from 41.6%-60% and its specificity only reported in 2 studies which was 100%.

^{68}Ga-DOTATATE PET/CT versus CT or MRI

There were 2 studies comparing the ^{68}Ga-DOTATATE PET/CT to MRI and 1 study comparing the ^{68}Ga-DOTATATE PET/CT to contrast enhanced CT (**Table 5**). The total number of patients in these studies were 56. In one of the studies the sensitivity and specificity of the ^{68}Ga-DOTATATE PET/CT was reported to be 93.8-100% whereas it was 92.6-100% respectively for MRI. In another study, sensitivity of MRI was reported to be 63.1%. No specificity of MRI was reported. No sensitivity or specificity in the CT study was calculated.

^{68}Ga-DOTATATE PET/CT versus ^{18}F-FDG PET/CT

There were 3 studies comparing the ^{68}Ga-DOTATATE PET/CT to ^{18}F-FDG PET/CT (**Table 6**). The total number of patients in these studies was 74. The sensitivity of the ^{68}Ga-DOTATATE PET/CT reported to be 72.2-100%. The sensitivity of the ^{18}F-FDG PET/CT reported to be 66-77.8%. No specificity of the ^{68}Ga-DOTATATE PET/CT or ^{18}F-FDG PET/CT was reported in these 2 studies.

Discussion

Somatostatin receptor-based imaging is the functional imaging of choice in diagnosis and management of NETs. The mechanism of somatostatin receptor-based radionuclide imaging is the binding of a radiolabeled ligand to the somatostatin receptor. The first investigation was published in 1984 by Reubi et al discussed the over expression of somatostatin receptors on tumor tissue [13]. Krenning et al in 1993 was the first to report the scintigraphy of NETs expressing somatostatin receptors using ^{123}I-Tyr-octreotide [14].

With availability of positron emitting tomography in recent years, PET tracers labeled somatostatin analogues have been developed rapidly. With the help of ^{68}Ge/^{68}Ga generators, now the PET radiolabelled tracers can be made on site independent of cyclotron and therefore less expensive for clinical practice. ^{68}Ga is eluted from the ^{68}Ge/^{68}Ga generator which immobilizes the parent radioisotope Germanium. There are several generators available in market including itm (Isotopen Technologien Muenchen AG), EZ (Eckert & Ziegler Strahlen- und Medizintechnik AG) and iThemba labs which differ in their construction and method of germanium immobilization. The Ga-68 can be eluted using various concentrations of HCl. Several different methods have been used for radiolabeling of DOTATATE with Ga-68, including preconcentration and purification (cationic or anion exchange) method or fractionation method based on the feasibility and type of generator. In few methods post-processing purification by using C-18 Sep Pak purification to ensure removal of free Ga-68. The quality control (including the endotoxin test, ^{68}Ge breakthrough, radionuclide identity test, osmolality test, pH test) of the ^{68}Ga-DOTATATE completes

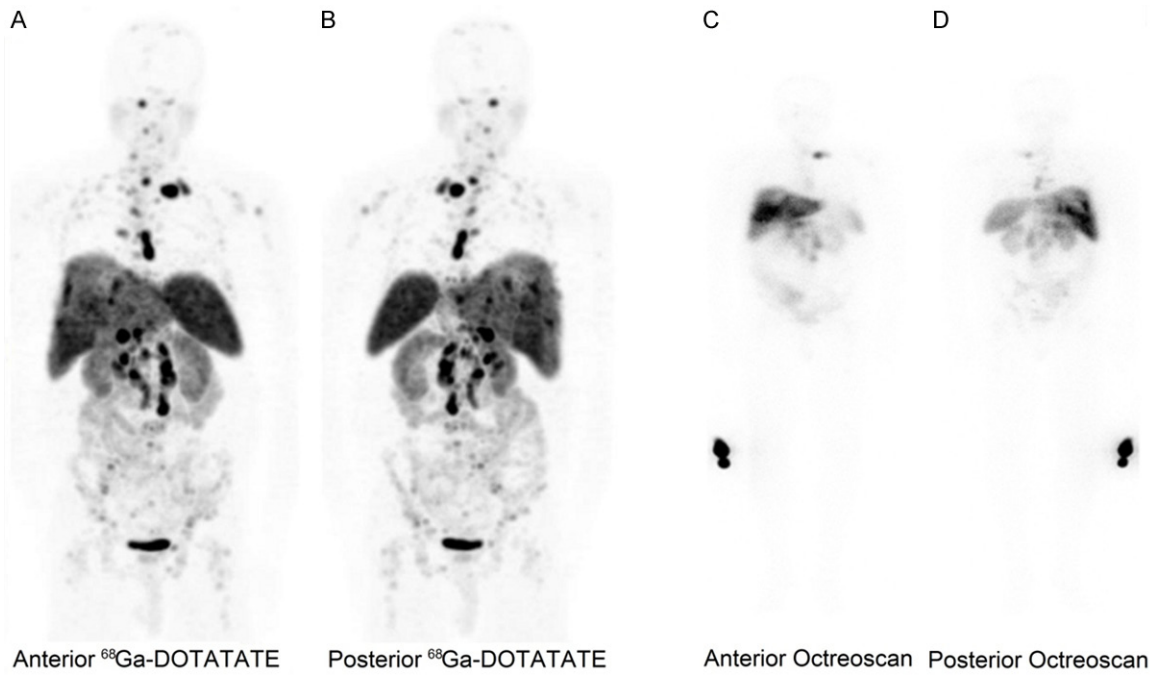

Figure 1. Side by side comparison of ^{68}Ga-DOTATATE to Octreoscan from one of our patients with neuroendocrine tumor. Anterior (A) and posterior (B) ^{68}Ga-DOTATATE pet images demonstrate extensive metastatic disease. Octreoscan anterior (C) and posterior (D) images from same patient demonstrate much fewer lesions indicating superior quality of PET/CT imaging.

preparation of clinical dose of radiotracer. Nevertheless, the methodology of preparation of ^{68}Ga-DOTATATE is well characterized and standardized for clinical practice upon stringent quality control testing [15]. Reubi et al. reported that the affinity of DOTATATE in binding SST2 to be approximately 10-fold higher than that of octreotide [16]. Souvatzoglou et al. showed that the additional accurate anatomical information provided by the CT component of PET/CT, can add significant value in the diagnosis and evaluation of therapy response due to functional and morphological information of the disease [17].

Haug et al was the first study that evaluated the role of ^{68}Ga-DOTATATE PET/CT in suspected neuroendocrine tumors and correlated it with gold standard pathology [18]. ^{68}Ga-DOTATATE PET/CT identified NET in 29 of the 36 cases and excluded the presence of a NET in 61 of the 68 non-NET patients, indicating a sensitivity of 81% and specificity of 90%. In another study Haug et al investigated the role of ^{68}Ga-DOTATATE PET/CT in detection of metastatic lesions in patients with neuroendocrine cancer and compared it to gold standard pathology [19]. ^{68}Ga-DOTATATE PET/CT helped to identify NET recurrence in 26 of 29 patients (sensitivity, 90%) and excluded the presence of recurrent NET in 28 of 34 patients (specificity, 82%). The accuracy calculated to be 86% (54 of 63). In gastroenteropancreatic NET (n = 45), the ^{68}Ga-DOTATATE PET/CT showed to be more sensitive, specific and accurate. In this subgroup, sensitivity was 94%; specificity was 89%; and accuracy was 91%.

Srirajaskanthan et al were the first group that compared the ^{68}Ga-DOTATATE to Octreoscan [20]. They evaluated the diagnostic and management role of ^{68}Ga-DOTATATE PET imaging in patients with neuroendocrine tumors and negative or equivocal findings on ^{111}In-DTPA-octreotide scintigraphy. They showed that ^{68}Ga-DOTATATE PET was positive in 41 of these 47 patients (87.2%). No false-positive lesions were identified. ^{68}Ga-DOTATATE PET identified significantly more lesions than ^{111}In-DTPA-octreotide scintigraphy (168 versus 27 respectively, $P < 0.001$). Hofman et al [12] studied the impact of ^{68}Ga-DOTATATE PET/CT for imaging neuroendocrine and other somatostatin expressing tumors and compared it to Octreoscan and conventional imaging. They demonstrated that 88% of ^{68}Ga-DOTATATE PET/CT studies

were abnormal. Compared with conventional and In-111 octreotide imaging, additional information was provided by ^{68}Ga-DOTATATE PET/CT in 68 and 83% of patients, respectively. **Figure 1** demonstrates side by side comparison of ^{68}Ga-DOTATATE to Octreoscan.

To investigate the change in clinical management, Srirajaskanthan et al and Hofman et al further analyzed their data to understand whether the additional information provided by ^{68}Ga-DOTATATE PET/CT resulted in change in clinical management of the patients. Srirajaskanthan et al demonstrated that ^{68}Ga-DOTATATE imaging changed the management in 70.6% of patients, who were subsequently suitable for peptide receptor-targeted therapy. Hofman et al also found that ^{68}Ga-DOTATATE PET/CT resulted in change in clinical management of 81% patients. Management impact was high (inter-modality change) in 47%, moderate (intra-modality change) in 10% and low in 41% (not assessable in 2%) of the patients. High management impact included directing patients to curative surgery by identifying a primary site and directing patients with multiple metastases to systemic therapy. Change in management impact included directing patients to curative surgery by identifying a primary site and directing patients with multiple metastases to systemic therapy.

Łapińska et al studied the somatostatin receptor expression in neuroendocrine cancers using ^{68}Ga-DOTATATE PET/CT [21]. ^{68}Ga-DOTATATE PET/CT detected the presence of the somatostatin receptor affinity in 50 of the 97 patients (51.5%). They concluded that ^{68}Ga-DOTATATE PET provides information on tumor cell receptors status, which has a significant bearing on planning targeted radionuclide therapy.

Win et al were the first that investigated the diagnostic value of ^{68}Ga-DOTATATE in neuroectodermal tumors [22]. They compared ^{68}Ga-DOTATATE to MIBG imaging in small group of patients with neuroectodermal tumors. They showed that ^{68}Ga-DOTATATE identified more lesions with higher uptake and better resolution compared to ^{123}I-MIBG. Out of 5 patients, two patients had negative ^{123}I-MIBG and positive ^{68}Ga-DOTATATE scans. One had a weakly positive ^{123}I-MIBG and a strongly positive ^{68}Ga-DOTATATE scan. One had a positive ^{123}I-MIBG and positive ^{68}Ga-DOTATATE scans. Maurice et al compared the performance of ^{68}Ga-DOTATATE PET/CT and ^{123}I-MIBG SPECT [23]. They noticed that in head and neck lesions, with the lesions in 4 patients being picked up by ^{68}Ga-DOTATATE and missed by ^{123}I-MIBG. On a per-lesion analysis, ^{68}Ga-DOTATATE was able to detect 167 lesions versus 128 lesions detected by CT/MRI and 111 by MIBG imaging. This demonstrated the superiority ^{68}Ga-DOTATATE in detecting lesions in all anatomical locations, and particularly bony lesions. They concluded that ^{68}Ga-DOTATATE should be considered as a first-line investigation in patients at high risk of PGL and metastatic disease, such as in the screening of carriers for mutations associated with familial PGL syndromes. Also they mentioned that, ^{68}Ga-DOTATATE should be preferred over ^{123}I-MIBG in patients with metastatic spread, particularly if the bone involvement, is suspected. In the study by Naji et al similar finding was observed and ^{68}Ga-DOTATATE PET was superior to Octreoscan [24]. They found that ^{68}Ga-DOTATATE PET showed tumor lesions in ten out of 12 patients with confirmed disease, while ^{123}I-MIBG showed lesions in five out of 12 patients. ^{68}Ga-DOTATATE and ^{123}I-MIBG detected a total of 30 lesions, of which 29/30 was positive with ^{68}Ga-DOTATATE and 7/30 with ^{123}I-MIBG. We also found higher incidence of SDHB positive results in patients with positive ^{68}Ga-DOTATATE.

Schmid-Tannwald et al compared the abdominal MRI with diffusion-weighted imaging to ^{68}Ga-DOTATATE PET/CT in detection of neuroendocrine tumors of the pancreas and correlated with gold standard pathology [25]. They found that of the NETs were detected in 8/23 (34.8%) and 9/23 (39.1%) on T2w images by observers 1 and 2, respectively. Detection rates of pancreatic NET with PET/CT (both observers: 23/23 = 100%) were significantly higher than with MRI ($p < 0.05$). Goel et al evaluated the role of ^{68}Ga-DOTATATE PET/CT for the detection of bone metastases in pediatric neuroendocrine tumors (NETs) and to compare it with contrast enhanced CT scan [26]. Compared with CT scan, ^{68}Ga-DOTATATE PET detected bone metastases at a significantly higher rate ($P = 0.0039$). On a per lesion analysis, out of a total of 225 lesions detected by ^{68}Ga-DOTATATE PET, only 84 lesions could be detected by CT scan. They concluded that ^{68}Ga-DOTATATE PET/CT is more useful than CECT scan for the early detec-

tion of bone metastases in pediatric NETs. Armbruster et al, compared dynamic contrast enhanced magnetic to ^{68}Ga-DOTATATE PET/CT and ^{18}F FDG PET/CT in patients with liver metastases from neuroendocrine tumors [27]. They observed that the lesion-to-background ratios of arterial plasma flow and arterial flow fraction of liver metastases correlated negatively with the lesion-to-background ratios of SUVmean derived from ^{68}Ga-DOTATATE PET/CT (r = j0.54, P G 0.001; r = j0.39, P G 0.001, respectively). However they correlated positively with the lesion-to-background ratios of SUVmean derived from ^{18}F-FDG-PET/CT (r = 0.51, P G 0.05; r = 0.68, P G 0.01, respectively). The lesion-to-background ratios of the DCE-MRI parameters extracellular mean transit time and extracellular volume correlated very weakly with the lesion-to-background ratios of SUVmean from ^{68}Ga-DOTATATE PET/CT, whereas venous plasma flow, total plasma flow, hepatic uptake fraction, and intracellular uptake rate showed no correlation between DCE-MRI and PET/CT. They concluded that, they were able to show some DCE-MRI parameters, especially the flow-related parameters, are correlated with SUV from PET/CT, whereas other parameters correlate poorly or not at all, suggesting that the combination of MR and PET may improve the diagnostic power compared with each technique individually and has the potential to provide additional functional information of the liver.

Neuroendocrine cancers are slow growing tumor and ^{18}F-FDG PET/CT is not commonly used for initial evaluation of the neuroendocrine cancers. Due to slow metabolic activity of the NETs in initial stages, they are not extremely avid on ^{18}F-FDG PET/CT. Opposite to this, they are avid for ^{68}Ga-DOTATATE which demonstrate high uptake because neuroendocrine tumors express significant SSR2. However in the late state of disease when the tumor characteristics changes from being well differentiated to poorly differentiated the uptake pattern will change. In this case the tumor and metastatic sites demonstrate low ^{68}Ga-DOTATATE uptake due to less expression of SSR2 and high ^{18}F-FDG PET/CT uptake. Kayani et al were the first to compare ^{68}Ga-DOTATATE PET/CT to ^{18}F FDG PET/CT [28]. They retrospectively reviewed the findings with ^{68}Ga-DOTATATE and ^{18}F-FDG imaging in 38 patients with primary or recurrent NET. The reported a sensitivity of 82% for ^{68}Ga-DOTATATE PET/CT and 66% for ^{18}F-FDG PET/. The sensitivity of combined ^{68}Ga-DOTATATE and ^{18}F-FDG PET/CT was 92% (35 of 38). There was greater uptake of ^{68}Ga-DOTATATE than ^{18}F-FDG in low-grade NET (median SUV 29 vs 2.9, P < .001). In high-grade NET there was higher uptake of ^{18}F-FDG over ^{68}Ga-DOTATATE (median SUV 11.7 vs 4.4, P 5.03). There was a significant correlation with predominant tumor uptake of ^{68}Ga-DOTATATE or ^{18}F-FDG and tumor grade on histology (P < .0001). Kayani et al published their second article comparing the ^{68}Ga-DOTATATE to ^{18}F-FDG PET/CT in Pulmonary Neuroendocrine Tumors [29]. They retrospectively reviewed 18 patients with primary and recurrent bronchial carcinoid tumors. They found that all typical carcinoids showed high uptake of ^{68}Ga-DOTATATE (SUVmax ≥ 8.2), but 4 of 11 showed negative or minimal ^{18}F-FDG uptake (SUVmax 1.7-2.9). All tumors of higher grade showed high uptake of ^{18}F-FDG (SUVmax ≥ 11.7), but 3 of 5 showed only minimal accumulation of ^{68}Ga-DOTATATE (SUVmax = 2.2-2.8). Neither case of diffuse idiopathic pulmonary neuroendocrine cell hyperplasia showed uptake of ^{68}Ga-DOTATATE or ^{18}F-FDG. Typical carcinoids showed significantly higher uptake of ^{68}Ga-DOTATATE and significantly less uptake of ^{18}F-FDG than did tumors of higher grade (P = 0.002 and 0.005). There was no instance of false-positive uptake of ^{68}Ga-DOTATATE, but there were 3 sites of ^{18}F-FDG uptake secondary to inflammation. ^{68}Ga-DOTATATE was superior to ^{18}F-FDG in discriminating endobronchial tumor from distal collapsed lung (P = 0.02). Conray et al compared the ^{68}Ga-DOTATATE to ^{18}F-FDG PET/CT in medullary thyroid carcinoma [30]. They found that ^{68}Ga-DOTATATE PET/CT detected disease in 13 of 18 patients and ^{18}F-FDG PET/CT in detected disease in 14 of 18 patients. As it was expected, ^{18}F-FDG revealed a total of 28 metastatic MTC regions and ^{68}Ga-DOTATATE 23 regions.

Conclusion

^{68}Ga-DOTATATE PET/CT provides incremental diagnostic information compared to Octreoscan, MIBG scintigraphy and conventional imaging. ^{68}Ga-DOTATATE also has been proved to have significant impact in management of patients with neuroendocrine tumors. Additional benefit of ^{68}Ga-DOTATATE PET/CT include patient convenience with short time acquisition and lower radiation exposure signifying the important role of ^{68}Ga-DOTATATE/CT in clinical

practice of neuroendocrine and other somatostatin-avid malignancies.

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