



# Comparative Analysis between DOTANOC Versus Computed Tomography in Assessment of Neuroendocrine Tumors

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## Abstract

**Introduction:** Diagnosis of Neuroendocrine Tumours (NET) is a continuously evolving sphere in imaging science. Starting from endoscopies, ultrasounds, and other imaging modalities, discernment of a tumour is possible by combining two imaging techniques. DOTANOC is one such modality which works on the affinity of binding to somatostatin receptors present on the NET cells. This study was carried out to compare Computerized Tomography (CT) & DOTANOC scans in gastric carcinoid and analyse the significance of both.

**Methodology:** This retrospective secondary data analysis was carried out among 67 patients classified under NET for a period of five years between 2015 and 2019. Comparison was made between CT and DOTANOC based on tumour grade and stage. Data was entered and analysed using Microsoft Excel spreadsheet.

**Results:** Majority of the participants were males (59.7%) and were above 50 years of age (71.2%). Among the metastatic tumours, 56% were identified by DOTANOC as compared to CT and the most favourable organ for metastasis was liver. Nodal staging showed significant upstaging of 54.9% and thereby proved DOTANOC to be a better parameter. Tumour staging also showed a predominate upstaging of 40.2% indicating DOTANOC having the upper hand in scan modalities.

**Conclusion:** The present study has shown that DOTANOC scans are more specific for staging of the disease based on tumour, node and metastasis, for better diagnosis, staging guides & appropriate treatment.

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**Keywords:** Computerized Tomography; DOTANOC; Gastric carcinoid; Neuroendocrine tumors.

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## Introduction

Gastric Neuroendocrine Tumors (GNET) are distinct entities characterized by hypergastrinemia arising from the enterochromaffin layer of the stomach. Although these tumors are rare, with an incidence of 1-2 per 100,000 population every year, the incidence rates significantly have been on the rise due to increased frequency of upper gastrointestinal endoscopy [1]. Yet another documented risk factor of GNET tumors include chronic use of proton pump inhibitors. Histopathologically, these tumors are classified into four types, in which type I tumors are more common and are associated with less mortality, as against type IV which is rare and has significantly high mortality.

The diagnosis of GNET has significantly evolved over the years. While these tumors were incidentally diagnosed by upper gastrointestinal endoscopy, several imaging modalities including ultrasound, Computerized Tomography (CT) and Positron Emission Tomography (PET) play a significant role in evaluating the extent of involvement and detection of metastasis. Further technological advances have proven that discernment of tumors are better when combining both PET & CT for a detailed imaging of the disease. With the development of PET-CT scans, tumour, lymph nodes, metastases can be identified distinctly without any scepticism by the doctors. DOTANOC is one such scan which works on the affinity of binding to somatostatin receptors present on the NET cells. The earliest somatostatin analog used for localization of GNET tumors was iodine 123 conjugated octreotide. However, in recent times, Gallium -68 DOTA-conjugated somatostatin analogs are widely being used of which DOTANOC is one of its kind [2].

It has been hypothesized that combined use of PET-CT using DOTANOC has better rates of detecting the tumor size, grade and stage in comparison with individual use of any of the imaging modalities. Although there are few studies evaluating the role of individual modality, there are very few studies to evaluate the combined benefit, in comparison with the gold standard CT investigation. Evaluation of these investigations to examine their validity will give deeper insights into the preferred choice of investigation and improve the quality of diagnosis, management and prognosis.

## Objectives

This study was carried out to evaluate the validity of DOTANOC in comparison with CT findings for detection of Gastrointestinal Neuroendocrine Tumors (GNET)

## Methodology

**Study setting and participants:** This retrospective secondary data analysis was carried out in the Department of Surgical Gastroenterology of our tertiary care hospital for a period of five years between 2015 and 2019. All the patients who underwent DOTANOC, PET and CT of the abdomen were taken up for the study. Data from 67 patients were analyzed for this study.

**Ethical approval:** Approval was obtained from the institutional ethics committee prior to the commencement of the study.

**Data collection:** Data regarding the tumor, node and metastasis (TNM) staging and grading of the tumors were carried out. TNM Staging was done based on standard American Joint Committee on Cancer (AJCC) criteria.

**Data analysis:** Data was entered and analyzed using Microsoft Excel spreadsheet 2010. The comparative staging and grad-

ing of the tumors were expressed in percentages.

## Results

Majority of the participants were males (59.7%) and were above 50 years of age (71.2%) (Table 1).

Most of the tumors belonged to grade 3(43.9%) followed by grade 1 (33.3%). The age-wise distribution of grading and focality of the tumors is given in Table 2.

On comparing the tumor staging between DOTANOC and CT scan images, it was observed that DOTANOC had better ability to diagnose the tumor stages compared to CT scan, especially in T1 (19% and 7% respectively) T3(42% and 40% respectively) and T4b(13% and 6% respectively). More importantly, about 30% of the lesions were not picked up by CT as compared to 11% by DOTANOC (Figure 1).

The number of cases with nodal involvement were 51 (76.1%). The nodal staging identified by both scan modalities was 10 cases (19.6%). The number of cases where downstaging occurred (CT scan) was 1 case (1.96%). The number of cases where upstaging occurred, indicating DOTA scan was 28 cases (54.9%) (Figure 2).

The total number of cases with metastasis was 50 (74.6%). The maximum number of cases were identified by 68Ga-DOTANOC scans in detecting metastasis to distant organs (M1). About 13 (19.4%) cases were identified by both scan modalities equally and CT scan alone identified 9 (13.4%) patients. The majority of the spread was in the liver (80%) followed by the pancreas, thyroid and other organs (Figure 3).

SuV values are computed based on the tumor size and injected dose. Mean values > 2 is indicative of malignancy. In this study, the SuV values for each grade of the tumors were computed. The mean SuV values were 7.05, for grade 2 9.46 and 8.68 for grade 1, 2 and 3 tumors respectively (Table 3).

The image finding from DOTANOC of perigastric nodes is given in Figure 4.

The comparative findings of metastasis between DOTANOC and CT scan are given in Figure 5 and 6.

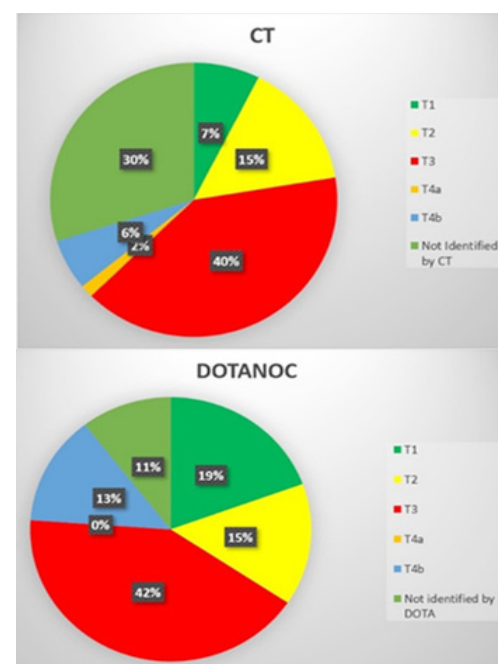


Figure 1: Tumor staging.

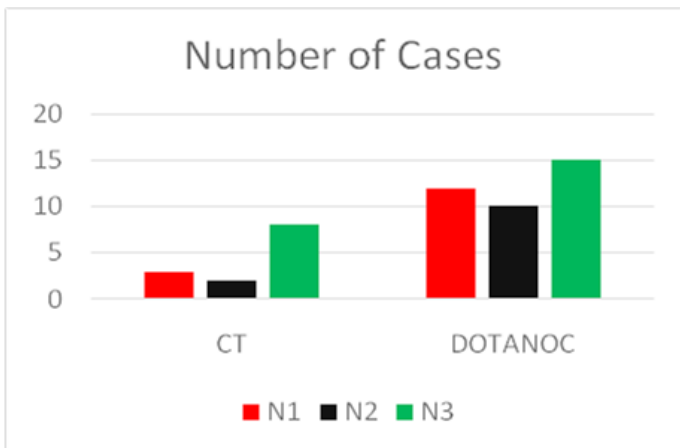


Figure 2: Nodal staging.

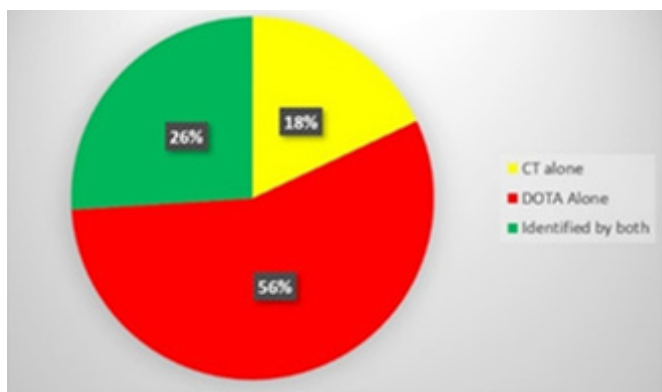


Figure 3: Metastasis staging.

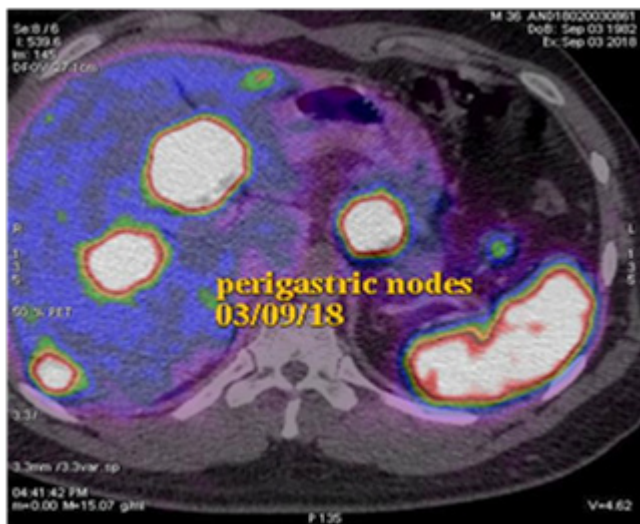


Figure 4: Perigastric nodes identified by DOTANOC.

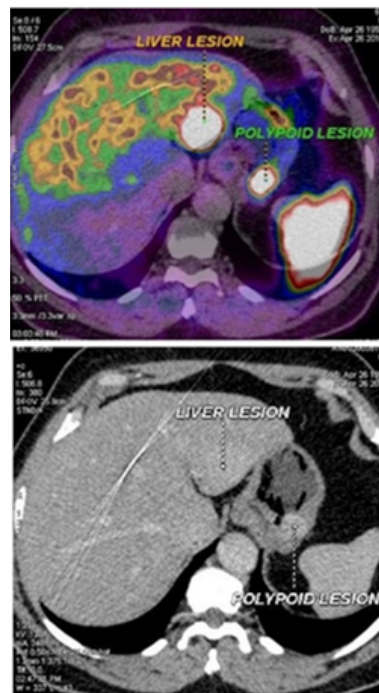


Figure 5: Detection of metastasis by DOTANOC and CT scan.

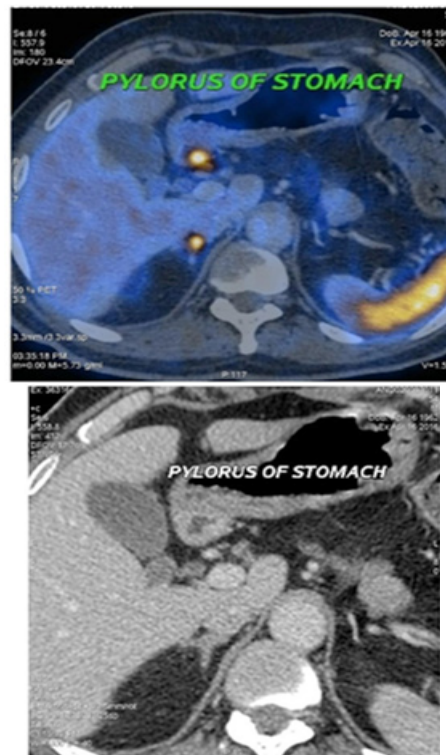


Figure 6: Comparison of metastasis in the pylorus of the stomach between DOTANOC and CT scan.

Table 1: Background characteristics of the study participants.

S. No	Characteristics	Frequency (n=67)	Percentage (%)
1	Age (in years)		
	>50	48	71.6
	<50	19	28.3
2	Sex		
	Males	40	59.7
	Females	27	40.3

Table 2: Tumor characteristics.

S. No	Characteristics	Age <50 years n(%)	Age >50 years n(%)	Total
1	Tumor grade			
	Grade 1	9 (40.9)	13 (59.1)	22
	Grade 2	6 (37.5)	10 (62.5)	16
	Grade 3	7 (25)	21 (75)	28

**Table 3:** SuV values based on the grading of tumors.

S. No	Characteristics	Grade 1	Grade 2	Grade 3
1	Mean	7.05	9.46	8.68
2	Median	6.9	8.5	7.5
3	Highest value	16	19	15
4	Lowest value	2	3	2

### Discussion

Neuroendocrine Tumors (NET) comprises of both nerve cells and hormone secreting cells. NET cells are malignant cells and can be classified based on the location where they are present. Most of them arise in the Gastro intestinal Tract. The tumors are then classified according to the TNM staging criteria. NET cells can be of different types including carcinoids. Gastric carcinoids constitute 4% of all gastrointestinal neuroendocrine tumors (GI-neuroendocrine tumors) and 1% of gastric neoplasms. The 5-year survival without metastasis ranges from 46% to 78%. The survival is poor with metastatic tumors. Neuroendocrine tumors are characterized by the presence and upregulation of serotonin receptors on its surface. There are five types of serotonin receptors namely SSTR 1 till SSTR 5. Based on the presence of the type of receptor, it is helpful for the diagnostic purposes done with the Ga-DOTANOC SCANS.

Gallium DOTA peptides include DOTATATE, DOTATOC & DOTANOC, each of which has different levels of affinities with the somatostatin receptors, out of which the most sensitive one is the DOTANOC scan especially to the SSTR 3 receptor. As of now, the preferred scanning modality appears to be PET-CT considering it is cost effective and can identify tumors to a certain extent.

The advantage of DOTA scans in identifying NET cells has been widely established. Prasad *et al.* found that Ga-68 DOTANOC PET/CT identified primary sites in 35 out of 59 patients (59%) and concluded that Ga-68 DOTANOC PET/CT is superior to In-111-OctreoScan [3]. Although, another study was done by Groshi MR et al to compare of DOTA scanning with PET-CT scanning for ACTH tumors, it was seen that contrast enhanced CT remains the first-line investigation in localization of these tumors [4]. A third study done by Naswa Net al proved that Gallium DOTANOC PET-CT appears to be very sensitive & was reported that reported that the sensitivity of <sup>68</sup>Ga-DOTANOC and <sup>18</sup>F-FDG was 91.4% and 42.5%, respectively and is therefore a specific mode of diagnosis of gastro pancreatic NET & thus better than conventional imaging [5]. Also, Koukouraki et al. demonstrated that the sensitivity of <sup>68</sup>Ga-DOTATOC and <sup>18</sup>F-FDG was 90% and 68%, respectively, and <sup>68</sup>Ga-DOTANOC was more sensitive in the detection of primary sites or metastasis than PET-CT scanning [8]. The results of this study compliments the results of our study where it is seen that <sup>68</sup>Ga-DOTANOC scans are much more efficient in the T,N& M staging of gastric carcinoid patients as compared to the PET-CT scanning technique.

Regarding the SUV values, the present study observed that a lower grade tumor had a higher SUV value which contradicts the statement that “more the malignancy, higher the SUV value”. The reason for this being sometimes a highly malignant cell can have a limited uptake and thus lower serotonin receptor expression, hence the low SuV value. This similar result was also seen in a study done by Chalermrat Kaeuputetal [6].

### Conclusion

The present study has emphasized the validity of DOTANOC scans in staging of neuroendocrine tumors. It may be established that DOTANOC scans can be routinely employed for staging of the disease based on tumour, node and metastasis, for better diagnosis, staging guides & appropriate treatment.

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