# Iodine-131 meta-iodobezylguanidine single photon emission computed tomography/ computerized tomography in diagnosis of neuro-endocrine tumors

**Chidambaram Natrajan Balasubramanian Harisankar, Bhagwant Rai Mittal, Anish Bhattacharya, Raghava Kashyap, Anil Bhansali[1]**

Departments of Nuclear Medicine and PET, and [1]Endocrinology, Postgraduate Institute of Medical Education and Research, Chandigarh, India

ABSTRACT

Metaiodobenzyl guanidine (MIBG) is a derivative of guanethidine and acts as an analogue of nor-epinephrine and is widely used in the imaging of tumors of neuro-endocrine origin. Iodine-123 MIBG has ideal imaging characteristics but is expensive with limited availability. Iodine-131 MIBG is widely used in India and is cheap. Hybrid single photon emission computed tomography (SPECT)/computerized tomography (CT) allows for anatomico-functional imaging and is being tried in MIBG studies. However, the experience with I-131 MIBG is limited. We present a pictorial assay of I-131 MIBG SPECT/CT findings in various MIBG avid tumors.

**Keywords:** Metaiodobenzyl guanidine, neuro-endocrine tumor, pheochromocytoma, single photon emission computed tomography/computerized tomography

## INTRODUCTION

Metaiodobenzyl guanidine (MIBG) is a derivative of guanethidine and acts as an analogue of nor-epinephrine. Therefore, it is concentrated in the sympatho-adrenergic tissues, especially in the chromaffin tissue of the adrenal medulla. Uptake of MIBG is both by passive diffusion and active uptake.[1] Cellular uptake of MIBG is followed by uptake in intracellular storage granules facilitated by vesicular monoamine transporters.[2] MIBG is labeled with either Iodine-123 (I-123) or Iodine-131 (I-131). Even though I-123 labeled MIBG is the radiopharmaceutical of choice for single photon emission computed tomography (SPECT) and in pediatric patients owing to favorable photon energy and lack of beta radiation, the availability of this radiopharmaceutical is limited especially in India. Most centers in India continue to use I-131 MIBG due to its lower cost and ready availability. Use of I-131 MIBG is complicated by high energy photons and beta decay which leads to sub-optimal imaging properties and higher radiation dose to the patient.

I-131 MIBG has been shown to localize in pheochromocytomas[3] including sporadic, benign intra-adrenal and extra-adrenal,[4]

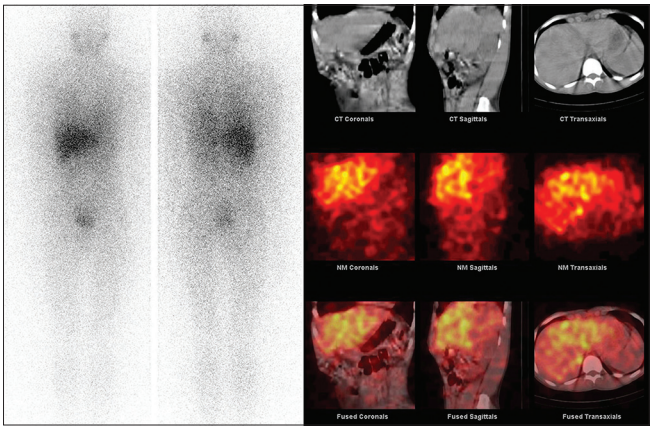


**Figure 1:** A 25-year-old male presented with hypertension for 10 years. Biochemically vesicular monoamine transporter (VMA) was borderline elevated. Computerized tomography (CT) of the abdomen was normal. Iodine-131 metaiodobenzyl guanidine (MIBG) whole body scintigraphy and single photon emission computed tomography/CT showed physiological distribution of MIBG. Patient is being clinically followed-up without evidence of neuro-endocrine tumor

Access this article online

Quick Response Code:

Website: www.ijnm.in

DOI: 10.4103/0972-3919.108877

**Address for correspondence:**
Dr. Bhagwant Rai Mittal, Department of Nuclear Medicine, PGIMER, Chandigarh - 160 012, India. E-mail: brmittal@yahoo.com

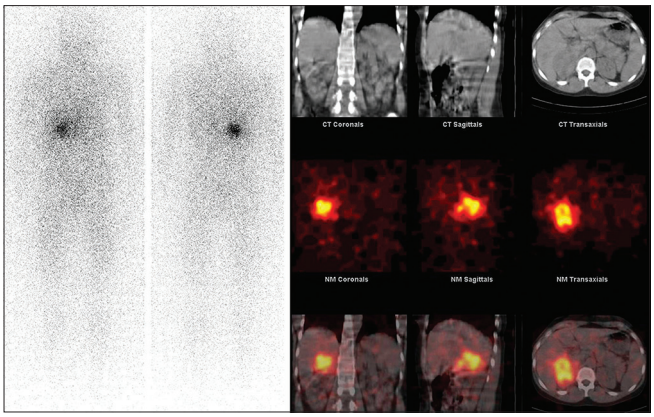


**Figure 2:** A 35-year-old male presented with palpitation and headache for 2 years. Urinary metanephrines were elevated. Contrast enhanced computed tomography (CECT) abdomen showed a right suprarenal mass. Iodine-131 metaiodobenzyl guanidine (MIBG) whole body scintigraphy and single photon emission computed tomography/computerized tomography showed MIBG avid enlarged right adrenal gland suggestive of functioning neuro-endocrine tumor. The tumor was surgically resected and histopathology revealed pheochromocytoma

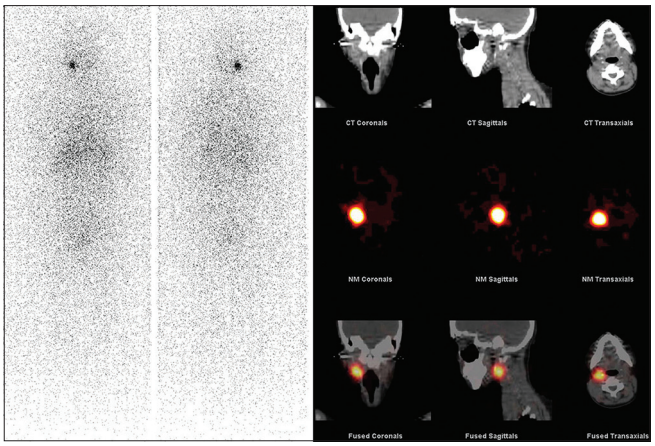


**Figure 3:** A 25 year with neck pain and a previous history of metastatic involvement of cervical lymph nodes by neuro-endocrine tumor was referred for Iodine-131 metaiodobenzyl guanidine (MIBG) study. The scan showed a focus of MIBG uptake in the right side of the neck. Single photon emission computed tomography/computerized tomography localized the uptake to the region of carotid artery bifurcation indicating carotid body tumor

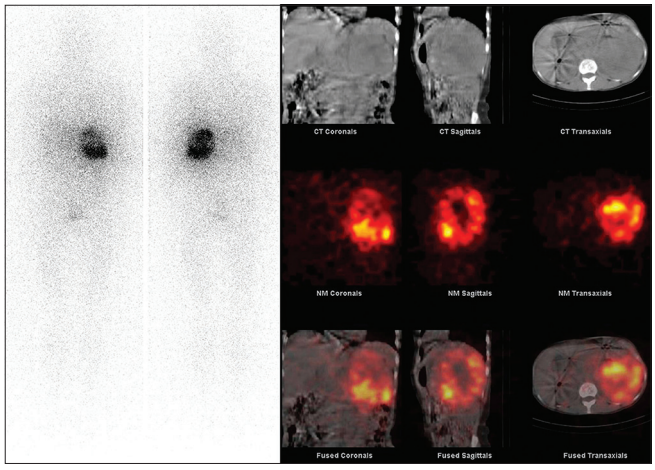


**Figure 4:** A 40-year-old female, known case of hypertension and type 2 diabetes mellitus presented with an adrenal mass. Urinary VMA was elevated. CECT abdomen showed a large left adrenal region mass with cystic areas. Iodine-131 metaiodobenzyl guanidine (MIBG) whole body scintigraphy and single photon emission computed tomography/computerized tomography showed MIBG avid functioning left adrenal neuro-endocrine tumor. The patient was operated upon and the mass excised and was proven to be cystic pheochromocytoma

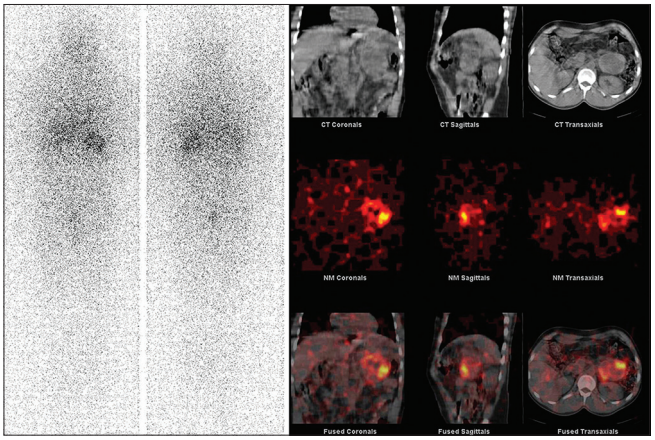


**Figure 5:** A 30-year-old male suspected to be a case of hydatid cyst (on ultrasonography) in the tail of pancreas developed accelerated hypertension upon handling of the mass inside the operation theatre. Surgery was abandoned. Iodine-131 metaiodobenzyl guanidine (MIBG) whole body scintigraphy and single photon emission computed tomography/computerized tomography performed showed MIBG avidity in the mass. Patient was subjected to repeat surgery and was proven to have neuro-endocrine tumor post operatively

familial[5] and malignant[6] neoplasms. Further, it is also used for initial evaluation, predicting response to therapy and detection of recurrence in neuroblastomas.[7] It is a useful tool in therapy of selected patients with medullary thyroid cancer[8] and carcinoid tumor.[9] I-131 MIBG is also used in therapy of variety of tumors showing avidity to MIBG. It was first developed for adrenal scintigraphy and its human use was first reported by Sisson *et al*.[10] The biodistribution of MIBG is characterized by uptake in normal liver, myocardium, salivary glands, intestines, spleen and excretion into urinary bladder. The normal adrenal medulla can be visualized with I-123 MIBG and more rarely with I-131 MIBG.[2] The finding of non-physiological uptake denote the presence of a neuro-endocrine tumor (NET). False-positives are very rare and can be due to obstruction to urinary tract or adrenal gland hyperplasia following unilateral adrenalectomy.[2]

Scintigraphy using I-131 MIBG has been reported to have a sensitivity of 77-90% and specificity of 95-100% in detection of pheochromocytomas/paragangliomas.[11,12] In general, the diagnostic accuracy of MIBG is lower in extra-adrenal and malignant paragangliomas.[13] Sub-optimal sensitivity of MIBG might be associated with relative lack of affinity to MIBG to the NET, lack of storage granules or loss of vesicular monoamine transporter (VMAT) due to tumor dedifferentiation.[14]

I-123 MIBG is a very important investigation in management of children with neuroblastoma and has been shown to have sensitivity of about 90% and specificity close to 100%.[15] I-131 MIBG is used as a therapeutic option in patients with advanced neuroblastomas. Approximately 60-70% of the carcinoids are visualized with MIBG. Better results are obtained for tumors originating from the midgut, whereas only 11% originating from the foregut are visualized with

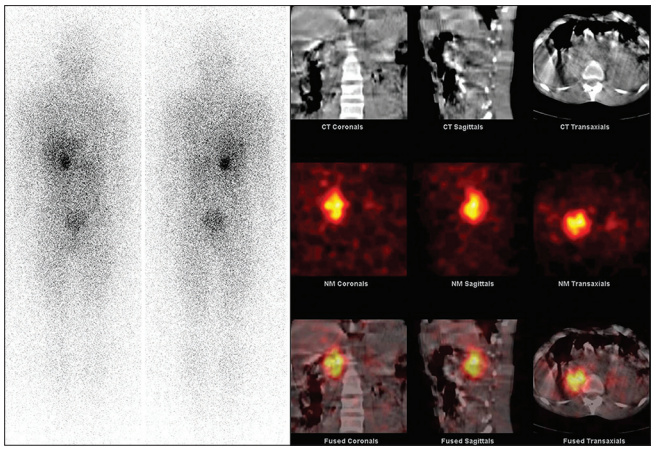


**Figure 6:** A 19-year-old male presented with accelerated hypertension and right adrenal mass. CECT showed a lobulated heterogenous right paracaval mass suggestive of extra-adrenal pheochromocytoma. Iodine-131 metaiodobenzyl guanidine (MIBG) whole body scintigraphy and single photon emission computed tomography/computerized tomography showed MIBG avid focus in the right suprarenal area. Histopathology revealed extra-adrenal pheochromocytoma

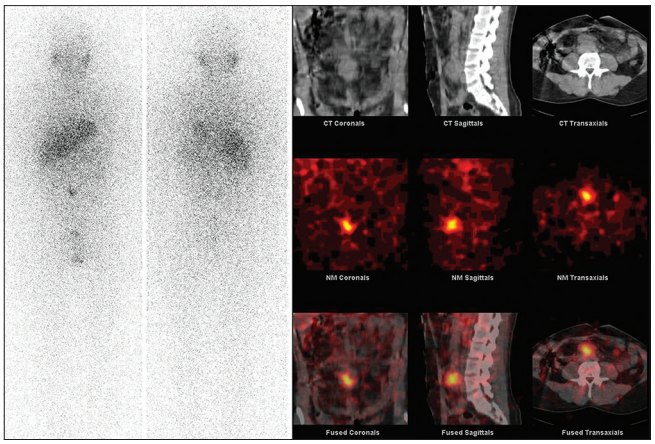


**Figure 7:** A 33-year-old male presented with abdominal pain and headache. Urinary metanephrines were elevated. Computerized tomography (CT) scan showed soft tissue density mass at the aortic bifurcation (organ of Zuckerkandl). Iodine-131 metaiodobenzyl guanidine (MIBG) whole body scintigraphy and single photon emission computed tomography/CT showed MIBG avid lesion in a soft tissue lesion at the level of L3-L4 vertebrae. Surgical removal was done and the mass proved to be paraganglioma

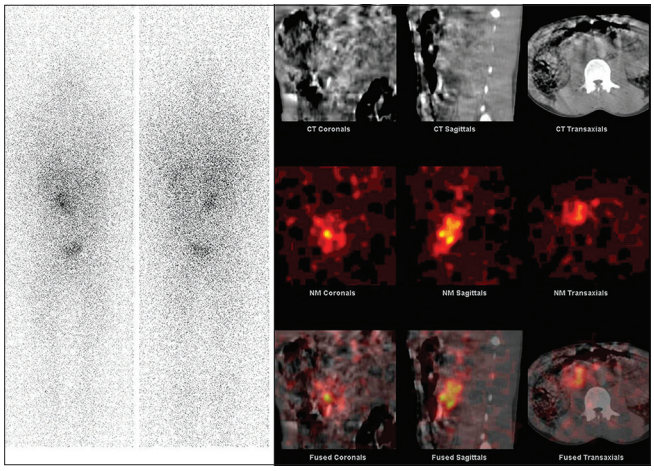


**Figure 8:** A 24-year-old male with history of hypertension for 5 years presented with elevated urinary VMA. Computerized tomography scan showed retroperitoneal lymphadenopathy with normal adrenal glands. Iodine-131 labeled metaiodobenzyl guanidine (MIBG) showed MIBG avid mass lesion in the right para-aortic region suggestive of functioning neuro-endocrine tumor which was later confirmed

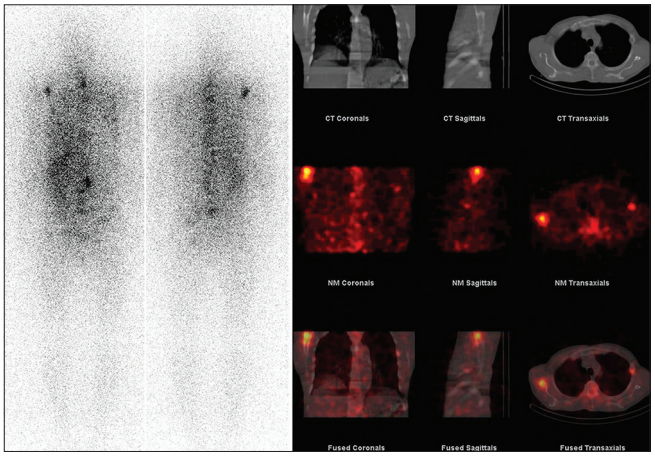


**Figure 9:** A 50-year-old male with hypertension and bony pains was referred for metaiodobenzyl guanidine (MIBG) study. Iodine-131 MIBG study with single photon emission computed tomography (SPECT)/Computerized tomography (CT) revealed MIBG avid lesions in the para-vertebral region and multiple vertebrae. SPECT/CT showed multiple areas of lytic changes in the visualized bones indicating widely metastatic pheochromocytoma. The patient was subjected to chemotherapy and had partial symptomatic relief

MIBG. Higher MIBG uptake is observed in concomitance with the elevated serotonin levels.[9] Medullary thyroid cancer shows variable avidity to MIBG with one study[8] showing a sensitivity of 38.7%. Lower sensitivity is because of very small size of the lesions. In spite of the lower sensitivity, MIBG avidity allows for radionuclide therapy of this rare malignancy.

The availability of hybrid SPECT/single photon emission computerized tomography (CT) has allowed for fusion imaging. Few studies have elaborated the role of SPECT/CT in MIBG studies[16-19] but the experience with I-131 MIBG SPECT/CT is limited. I-131 MIBG is the only choice in countries where I-123 MIBG is unavailable. I-131 MIBG SPECT/CT patterns in various MIBG avid lesions are pictorially depicted in this study.

## MATERIALS AND METHODS

Scintigraphic images of 11 patients [Figures 1-11] who underwent Iodine-131 MIBG are represented in this pictorial essay.

All patients underwent whole body scinitigraphy and hybrid SPECT/CT images of the involved sites. Whole body images were acquired 48 h after intravenous injection of 0.5 mCi to 1 mCi of iodine-131 labeled MIBG (I-131 MIBG). Patients were asked to discontinue any medication interfering with I-131 MIBG uptake before the study. Patients were administered syrup collosol iodine (25 ml/day; 8 mg/5 ml) the day before and 4 days after I-131 MIBG injection to block thyroid uptake of any free iodine.

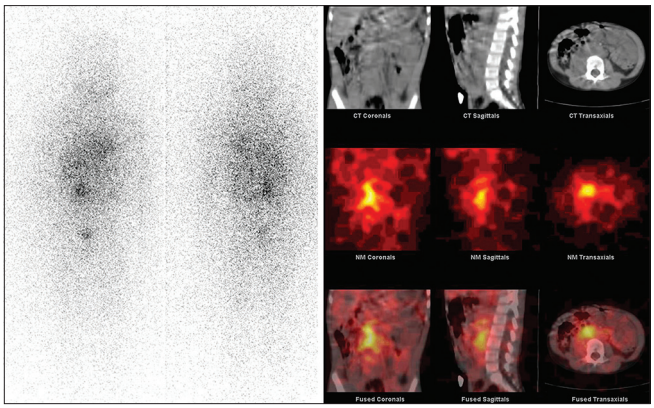


**Figure 10:** A 2½-year-old male child, known case of spinal ganglioneuroblastoma with elevated VMA and MRI evidence of right paravertebral mass post chemotherapy was referred for restaging. Iodine-131 metaiodobenzyl guanidine (MIBG) whole body scintigraphy and single photon emission computed tomography/computerized tomography showed MIBG avid tumor in the right paravertebral region opposite L1-L4 vertebrae suggestive of residual disease

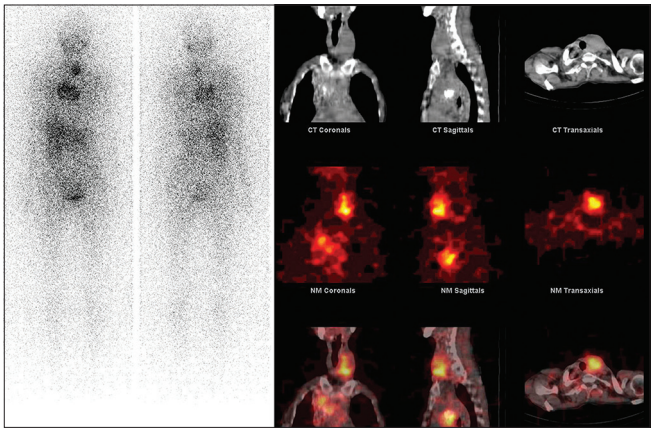


**Figure 11:** A 52-year-old female known case of MEN2A with status post excision of pheochromocytoma was referred for Iodine-131 metaiodobenzyl guanidine in view of elevated calcitonin. The scan showed increased tracer uptake in the neck and thorax. Hybrid single photon emission computed tomography/computerized tomography images localized the uptake to the enlarged left lobe of thyroid gland and calcified lesions in the anterior mediastinum, likely due to medullary thyroid carcinoma with mediastinal lymph nodal metastases which was confirmed later

All images were acquired in Infina Hawkeye 4 SPECT/CT scanner (GE Healthcare, Milwaukee, USA) fitted with a medium energy general purpose collimator. The whole body images were acquired at a speed of 10 cm/min. SPECT images were acquired in 64 × 64 matrix, in a step and shoot method covering 360 degrees in 60 views and 30 s per view. Following the SPECT acquisition, CT was acquired in helical mode and tube current of 2.5 mA covering the involved area. Images were transferred to Xeleris workstation and were evaluated. Hybrid SPECT/CT images were examined by evaluating the individual SPECT images, CT images and the fused SPECT/CT images.

## REFERENCES


1. Jaques S Jr, Tobes MC, Sisson JC. Sodium dependency of uptake of norepinephrine and m-iodobenzylguanidine into cultured human pheochromocytoma cells: Evidence for uptake-one. Cancer Res 1987;47:3920-8.
2. Bombardieri E, Coliva A, Maccauro M, Seregni E, Orunesu E, Chiti A, *et al.* Imaging of neuroendocrine tumours with gamma-emitting radiopharmaceuticals. Q J Nucl Med Mol Imaging 2010;54:3-15.
3. McEwan AJ, Shapiro B, Sisson JC, Beierwaltes WH, Ackery DM. Radio-iodobenzylguanidine for the scintigraphic location and therapy of adrenergic tumors. Semin Nucl Med 1985;15:132-53.
4. Shapiro B, Copp JE, Sisson JC, Eyre PL, Wallis J, Beierwaltes WH. Iodine-131 metaiodobenzylguanidine for the locating of suspected pheochromocytoma: Experience in 400 cases. J Nucl Med 1985;26:576-85.
5. Valk TW, Frager MS, Gross MD, Sisson JC, Wieland DM, Swanson DP, *et al.* Spectrum of pheochromocytoma in multiple endocrine neoplasia. A scintigraphic portrayal using 131I-metaiodobenzylguanidine. Ann Intern Med 1981;94:762-7.
6. Shapiro B, Sisson JC, Lloyd R, Nakajo M, Satterlee W, Beierwaltes WH. Malignant phaeochromocytoma: Clinical, biochemical and scintigraphic characterization. Clin Endocrinol (Oxf) 1984;20:189-203.
7. Boubaker A, Bischof Delaloye A. Nuclear medicine procedures and neuroblastoma in childhood. Their value in the diagnosis, staging and assessment of response to therapy. Q J Nucl Med 2003;47:31-40.
8. Castellani MR, Seregni E, Maccauro M, Chiesa C, Aliberti G, Orunesu E, *et al.* MIBG for diagnosis and therapy of medullary thyroid carcinoma: Is there still a role? Q J Nucl Med Mol Imaging 2008;52:430-40.
9. Khan MU, Morse M, Coleman RE. Radioiodinated metaiodobenzylguanidine in the diagnosis and therapy of carcinoid tumors. Q J Nucl Med Mol Imaging 2008;52:441-54.
10. Sisson JC, Frager MS, Valk TW, Gross MD, Swanson DP, Wieland DM, *et al.* Scintigraphic localization of pheochromocytoma. N Engl J Med 1981;305:12-7.
11. Sisson JC, Shulkin BL. Nuclear medicine imaging of pheochromocytoma and neuroblastoma. Q J Nucl Med 1999;43:217-23.
12. Furuta N, Kiyota H, Yoshigoe F, Hasegawa N, Ohishi Y. Diagnosis of pheochromocytoma using 123I -compared with 131I -metaiodobenzylguanidine scintigraphy. Int J Urol 1999;6:119-24.
13. Bhatia KS, Ismail MM, Sahdev A, Rockall AG, Hogarth K, Canizales A, *et al.* 123I-metaiodobenzylguanidine (MIBG) scintigraphy for the detection of adrenal and extra-adrenal phaeochromocytomas: CT and MRI correlation. Clin Endocrinol (Oxf) 2008;69:181-8.
14. Eisenhofer G. The role of neuronal and extraneuronal plasma membrane transporters in the inactivation of peripheral catecholamines. Pharmacol Ther 2001;91:35-62.
15. Boubaker A, Bischof Delaloye A. MIBG scintigraphy for the diagnosis and follow-up of children with neuroblastoma. Q J Nucl Med Mol Imaging 2008;52:388-402.
16. Tang HR, Da Silva AJ, Matthay KK, Price DC, Huberty JP, Hawkins RA, *et al.* Neuroblastoma imaging using a combined CT scanner-scintillation camera and 131I-MIBG. J Nucl Med 2001;42:237-47.
17. Rozovsky K, Koplewitz BZ, Krausz Y, Revel-Vilk S, Weintraub M, Chisin R, *et al.* Added value of SPECT/CT for correlation of MIBG scintigraphy and diagnostic CT in neuroblastoma and pheochromocytoma. Am J Roentgenol 2008;190:1085-90.
18. Meyer-Rochow GY, Schembri GP, Benn DE, Sywak MS, Delbridge LW, Robinson BG, *et al.* The utility of metaiodobenzylguanidine single photon emission computed tomography/computed tomography (MIBG SPECT/CT) for the diagnosis of pheochromocytoma. Ann Surg Oncol 2010;17:392-400.
19. Fukuoka M, Taki J, Mochizuki T, Kinuya S. Comparison of diagnostic value of I-123 MIBG and high-dose I-131 MIBG scintigraphy including incremental value of SPECT/CT over planar image in patients with malignant pheochromocytoma/paraganglioma and neuroblastoma. Clin Nucl Med 2011;36:1-7.


**How to cite this article:** Harisankar CB, Mittal BR, Bhattacharya A, Kashyap R, Bhansali A. Iodine-131 meta-iodobezylguanidine single photon emission computed tomography/computerized tomography in diagnosis of neuro-endocrine tumors. Indian J Nucl Med 2012;27:55-8.

**Source of Support:** Nil. **Conflict of Interest:** None declared.