

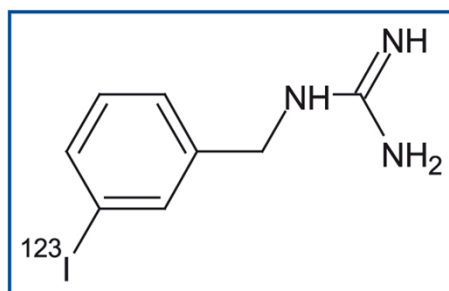
*IAEA Regional Training Course (AFRA) on the Role of
Nuclear Medicine in Endocrine Disease and
Infection/Inflammation*

Clinical Value of Imaging NETs with Radiolabeled MIBG

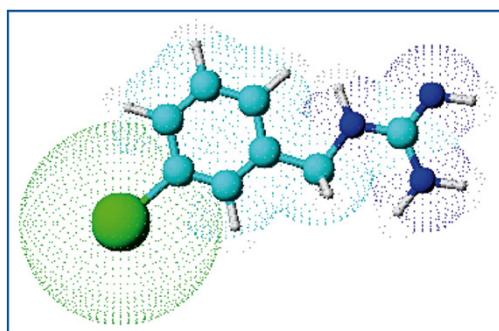
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Italy



Pretoria, South Africa, Dec. 6-10, 2010



[¹²³I]MIBG



[*I]MIBG

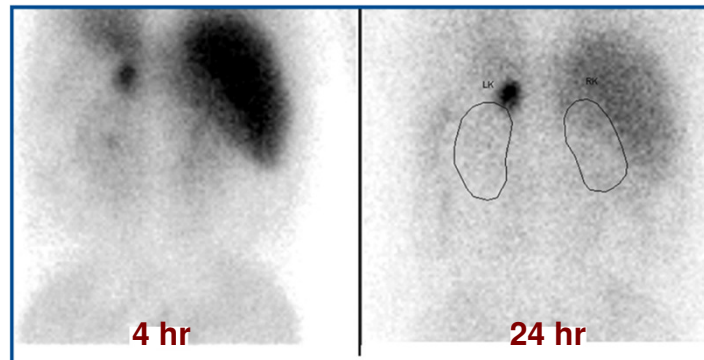
- As an analog of catecholamines, this false neurotransmitter accumulates in the neurosecretory vesicles of chromaffin cells.
- It enters chromaffin cells and the secretory vesicles through an active, ATP-dependent membrane transport (“uptake-1”).
- It does not bind to post-synaptic receptors.
- It is not degraded by COMT or MAO.
- Secretory vesicles are abundant in several tissues with adrenergic innervation.

Primary Clinical Indications to MIBG Scintigraphy

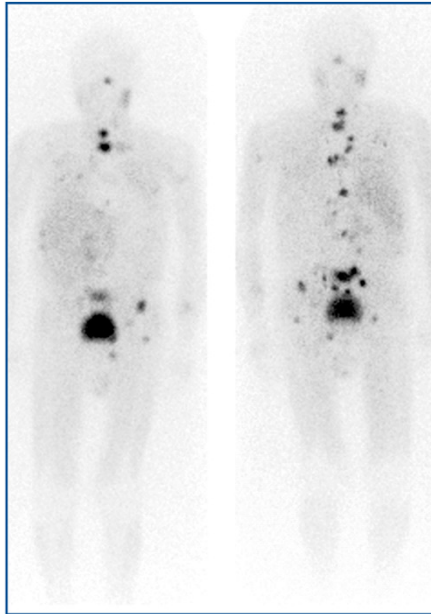
- Pheochromocytoma
- Paraganglioma
- Neuroblastoma
- Carcinoid tumors
- Medullary thyroid cancer
- Small cell lung cancer (SCLC)

[*I]MIBG Scintigraphy

- Thyroid-blocking medications.
- Discontinuation of drugs that interfere with catecholamine metabolism: typical and atypical antidepressants, reserpin, labetolol, metoprolol, cocaine, calcium-channel blockers.
- Slow i.v. infusion (possible mass effect).
- Monitoring of heart rate/blood pressure.
- i.v. α - or β -blockers if needed.
- Imaging starts 4-6 hours post-injection.



Although the relatively fast kinetics of [125 I]MIBG uptake in tumors makes imaging possible at 4-6 hr, delayed imaging improves target/bckg ratios (faster washout from non-specific sites, such as the kidney/urinary tract).



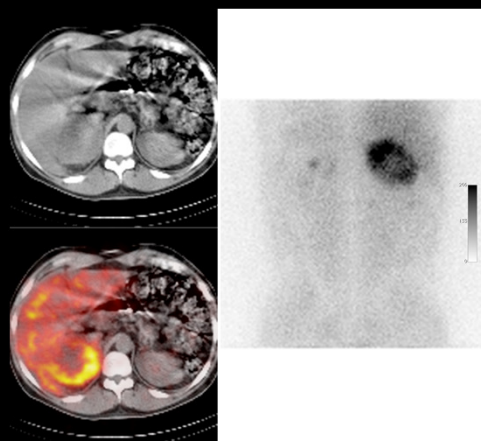
In addition to spot images, whole-body imaging is always useful for detecting distant metastases and for assessing the overall tumor burden

Drug	Mechanism	Suggested withdrawal prior to [¹²⁵I]MIBG
Opioids, cocaine, tramadol	Uptake inhibition	7-14 days
Tricyclic antidepressants	Uptake inhibition	7-21 days
Sympathomimetics	Depletion	7-14 days
Cardiovascular agents: labetalol, metoprolol, amiodarone	Uptake inhibition and depletion	21 days
Reserpine, bretylium, guanethidine	Depletion and transport inhibition	14 days
Verapamil and ACEI	Increased uptake and retention	5-7 days
Antipsychotics: phenothiazines, thioxanthenes, butyrophenones	Uptake inhibition	21-28 days

Clinical Impact of MIBG Scintigraphy (especially for pheochromocytomas)

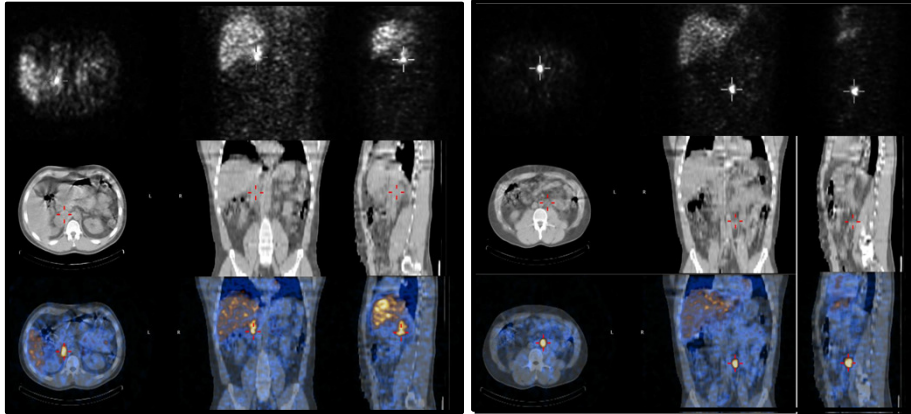
- Useful for detecting extra-adrenal lesions (better than CT and/or MR).
- Useful detecting residual and/or recurrent intra-abdominal disease after surgery.
- Useful for detecting distant metastases.
- Useful for selecting patients for [^{131}I]MIBG therapy.
- Useful for guiding resection of recurrent disease (intraoperative gamma probes).

[^{123}I]MIBG Scintigraphy in Pheochromocytoma



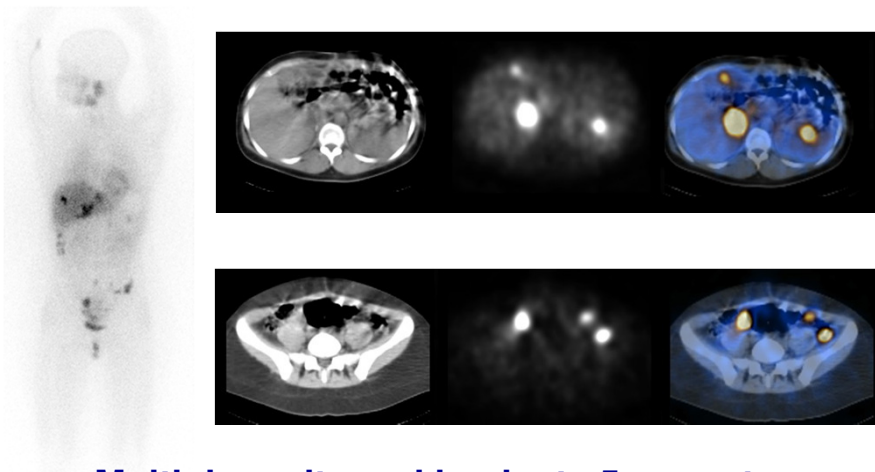
Bulky tumor of the right adrenal (central necrosis) with compensatory hyperplasia of left adrenal

SPECT/CT with [¹²³I]MIBG: arterial hypertension, increased catecholamines, and undefined mass in right adrenal



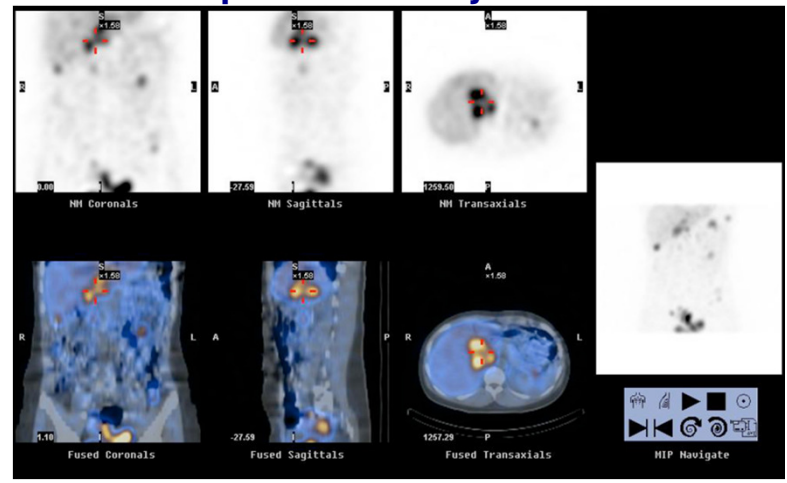
Increased uptake in right adrenal pheochromocytoma and in metastatic left para-aortic lymph nodes

SPECT/CT with [¹²³I]MIBG: recurrent pheochromocytoma



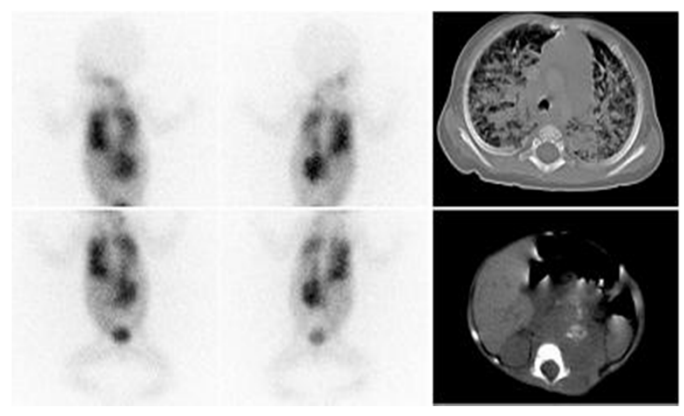
Multiple peritoneal implants 5 yr post-surgery (“benign” pheochromocytoma)

SPECT/CT with [¹²³I]MIBG: recurrent pheochromocytoma



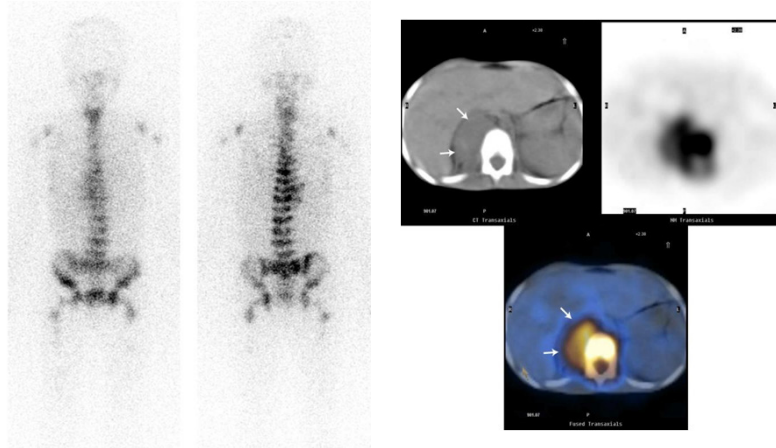
Multiple peritoneal implants 5 yr post-surgery (“benign” pheochromocytoma)

[¹²³I]MIBG Scintigraphy in Neuroblastoma



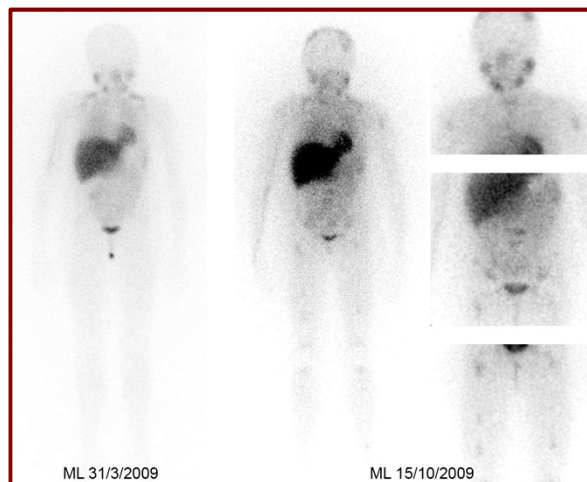
CT: diffuse interstitial abnormalities (uncertain).
[¹²³I]MIBG: diffuse lung metastases from retro-peritoneal neuroblastoma (stage 4).

[¹²³I]MIBG Scintigraphy in Neuroblastoma

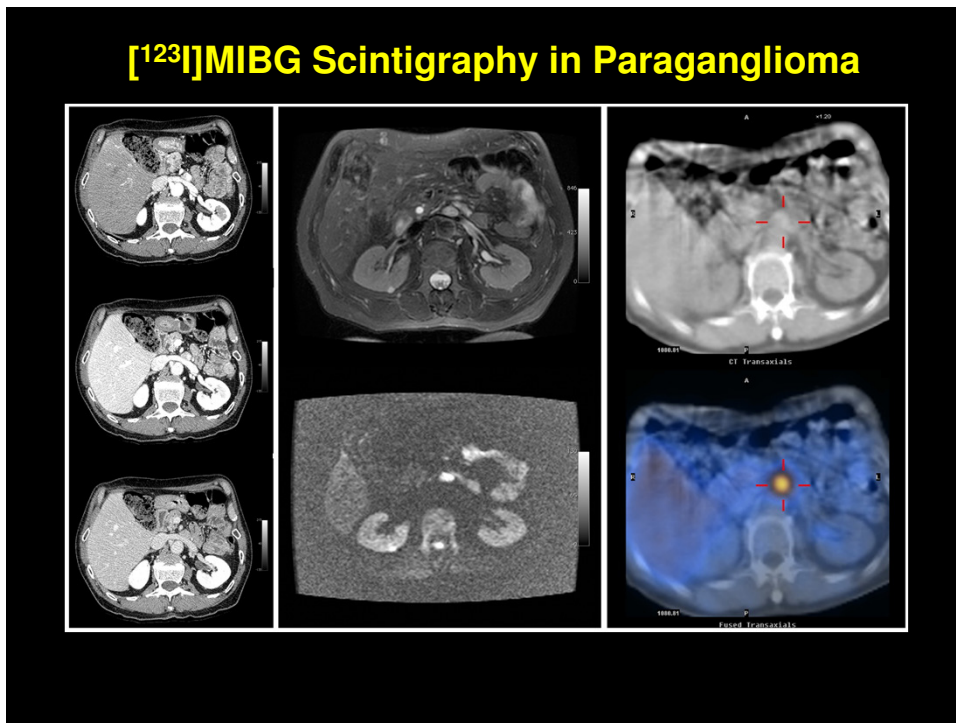


Diffuse metastatic osteo-medullary involvement that in the whole-body scan almost masks the primary lesion, which is instead clearly visualized on SPECT/CT.

[¹²³I]MIBG Scintigraphy in Neuroblastoma



**March 2009: complete response to chemotherapy.
 October 2009: recurrent disease in the skull, humera, sternum, spine, pelvis, femurs, tibiae.**



2008: 17-yr-old male with arterial hypertension, polycytemia, and increased urinary catecholamines. CT/MR: multiple retroperitoneal masses

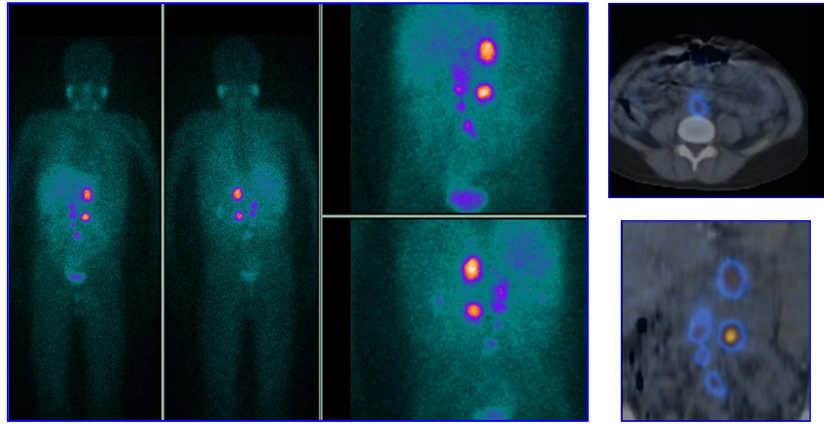
MR

CT

Octreoscan®

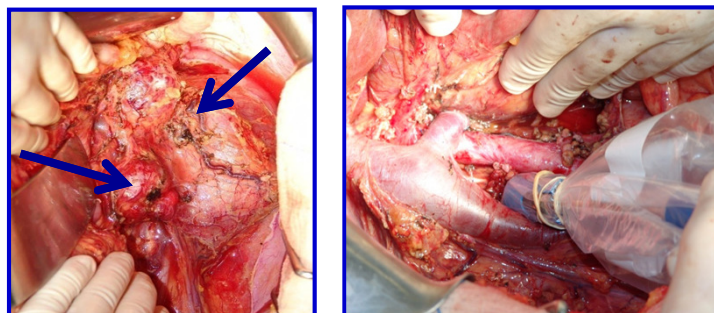
WBS 6 h

Static Addome 6 h



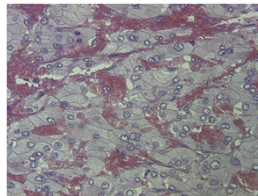
[¹²³I]MIBG: multiple focal areas of abnormal uptake in para-aortic region bilaterally, extending from the diaphragm to iliac bifurcation

Radioguided surgery (Neo2000 Bluetooth gamma probe) about 24 hr post-injection of 185 MBq [¹²³I]MIBG



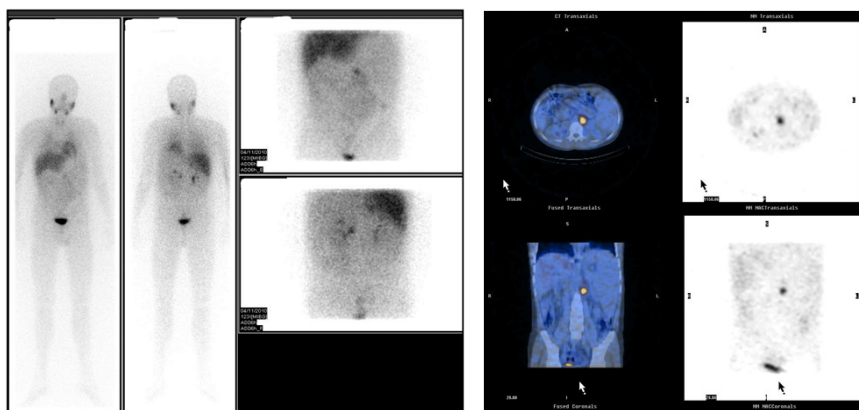
Resection of all para-aortic masses, visible and/or detected by intraoperative gamma counting

	<i>In-vivo</i>	T/B	<i>Ex-vivo</i>
Left para-aortic below diaphragm	31	1,5	96
Left aorto-iliac carrefour	102	5	388
Right para-aortic, paracaval	142	7	240
Right para-aortic, retrocaval at origin of upper mesenteric artery	265	12,5	300
Pre-left adrenal	92	4,4	275
Background	21		




Multiple paragangliomas 1 to 5.5 cm in size

2010: Recurring signs and symptoms



[¹²³I]MIBG: left para-aortic lesion

**Nov. 19, 2010: Radioguided surgery about 9hr
post-injection of 90 MBq [¹²³I]MIBG**

	Counts on SPECT	T/B	<i>In-vivo</i>	T/B	<i>Ex-vivo</i>
Left para-aortic close to left renal artery	163	5.1	450	5.0	380
Background	32		90		