Imaging Of Neuroendocrine Tumors

OVERVIEW: Neuroendocrine Tumor Imaging

Users of this tutorial will learn how to name the three radiopharmaceuticals suitable for use in detection of neuroendocrine tumors and their required storage conditions; will be able to list the most common indications for ordering this test; will be able to state the prescribed injected dose for each; will be able to describe patient preparation and thyroid blockage (as required) for each of these drugs; will be able to state the time and imaging parameters for planar and SPECT imaging; will be able to identify the sites of localization of each drug in a normal patient and will be able to identify neuroendocrine tumors on scans typical of the disease.

Radiopharmaceuticals Utilized in Neuroendocrine Tumor Imaging

- I-123 mIBG and I-131 mIBG
- In-111-Octreoscan (In=111-Pentetreotide)

Imaging of neuroendocrine tumors with I-123 mIBG and I-131 mIBG

INDICATIONS FOR CLINICAL STUDIES

- Pheochromocytoma
- Neuroblastoma
- Paraganglioma
- Medullary carcinoma of the thyroid
- Carcinoid tumors
- Medullary hyperplasia of adrenals

EPIDEMIOLOGY

- 0.1-0.5% of all hypertensives have a pheochromocytoma
- Occurs in both sexes at all ages. The younger the patient, the more likely the disease is familial
- Neuroblastoma is the second leading cause of death in children due to cancer
- Epidemiology
- Family history of certain syndromes associated with high incidence of pheochromocytoma, e.g., Neurofibromatosis, Multiple Endocrine Neuroplasia Syndrome (MEN), Von-Hipple Lindau disease

DIAGNOSTIC PATTERNS

- Family History
- Symptoms
- Clinical Data, for example
- Sustained or labile hypertension, unusually severe, markedly labile spells
- Hypertension plus spells (include sweating, palpitations, headache)

THE 10% RULE FOR PHEOCHROMOCYTOMAS

- 10% Multiple
- 10% Extra Adrenal
- 10% Bilateral
- 10% Familial
- 10% Malignant

PROCEDURES THAT EXPLORE ANATOMICAL SITES

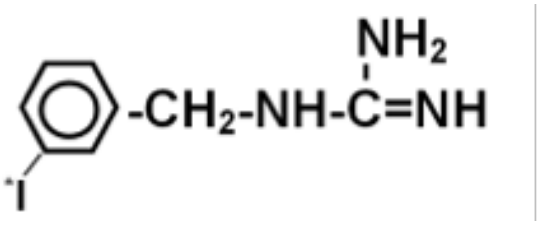
- Computed Tomography and MRI
- Ultrasound
- Scintigraphy with *I-mIBG or 111In Octreoscan
- Arteriogram guided by norepinephrine level
- Norepinephrine levels from different sites of vena cava

DRUG AVAILABILITY

I-123 mIBG: NDA Approved; available in US as of December 2008

I-131 mIBG: NDA Approved; available in US as of June, 1994

*I-mIBG STRUCTURE



CHARACTERISTICS OF I-123 and I-131

- t_{phys} of I-123 = 13.3 hr; E_γ = 159 keV
- t_{phys} of I-131 = 8.08 days; E_γ = 364.5 keV

PATIENT PREPARATION FOR I-mIBG INJECTION

- Thyroid Blockage with SSKI
- For I-123 mIBG, ten drops at least 30 minutes prior to injection of mIBG and three drops once a day for three days
- For I-131 mIBG, ten drops at least 30 minutes prior to the scan and three drops once a day for ten days
- Patient must drink extra fluid for 24 hr post injection to minimize radiation dose to urinary bladder and gonads

TYPICAL ADMINISTERED DOSE FOR ADULTS

- For I-123 -mIBG: 5-10 mCi
- For I-131-mIBG: 0.5 mCi

DRUG ADMINISTRATION PROCEDURE

- Inject over a two minute period
- Use a saline flush to keep butterfly open
- Observe patient for 20 min post injection to insure adverse reaction has not occurred
- Release patient

IMAGING TIMES

- For I-123 mIBG: whole body scan and posterior abdominal view at 24 hr post injection; posterior abdominal view at 36-40 hr post injection
- For I-131 mIBG: whole body scan and posterior abdominal view at 48 hr post injection; posterior abdominal view at 72 hr post injection

ADVERSE REACTIONS FOLLOWING IV INJECTION OF *I-mIBG

At our university, we have injected >1,000 patients with no recorded adverse reactions

CONTRAINDICATIONS: DRUGS THAT BLOCK UPTAKE OF mIBG

- Cocaine
- Reserpine Alkaloids
- Labetalol
- Phenylpropanolamine
- Tricyclic Antidepressants

NORMAL DISTRIBUTION OF *I-mIBG

- Myocardium
- Uptake is inversely proportional to circulating catecholamine levels
- Liver
- Adrenals
- Salivary glands
- Bowel (occasionally)

RADIATION DOSIMETRY OF I-131 -mIBG

ORGAN	RADS / 0.5 mCi
Adrenal Cortex	0.5
Adrenal Medulla	69.0
Kidneys	0.2 each
Liver	0.2
Ovaries and Testes	0.2
Pancreas	0.3
Spleen	0.7
Thyroid-Unblocked	17.3
Thyroid- Blocked	<1.0
Whole Body	0.1

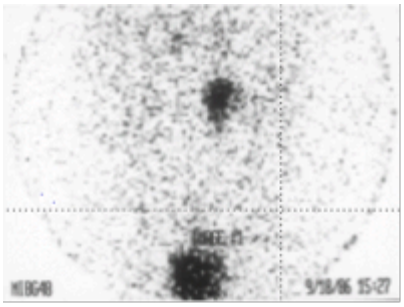
Clinical Cases: Neuroendocrine Tumor Imaging with I-123 mIBG and I-131 I mIBG

Conclusions

- Image quality of I-123 mIBG is superior to that obtained using I-131 mIBG
- Image time significantly reduced with I-123
- Sensitivity and specificity are both >90%

Clinical Study # 1: Patient WW

- 55 y/o WM, right adrenal mass on MRI
- history of HTN X 15 yr
- thyroid blocked with SSKI solution
- injected with 0.5 mCi of I-131 mIBG



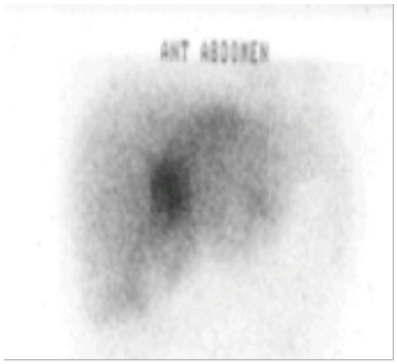
Clinical Study # 2: Patient EF

■ 44 y/o BF

■ History of HTN, anxiety

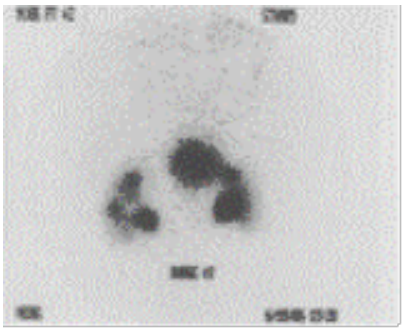
■ thyroid blocked with SSKI solution

■ injected with 10.5 mCi of I-123 mIBG



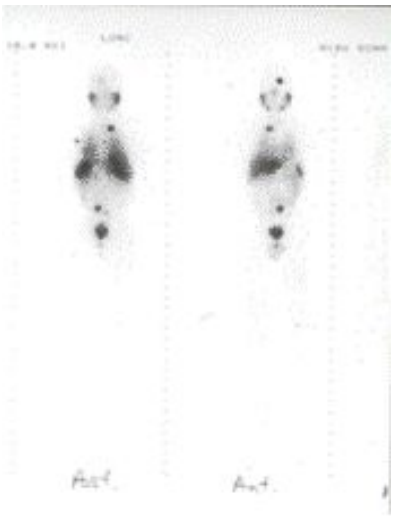
Clinical Study # 3: Patient SA

- thyroid blocked with KClO4
- 16y/o obese WF, R adrenal mass on CT
- history of HTN X several months
- elevated urinary catecholamines
- Medication: dibenzylene, 10 mg q 6 hr
- injected with 8.5 mCi of I-123 mIBG



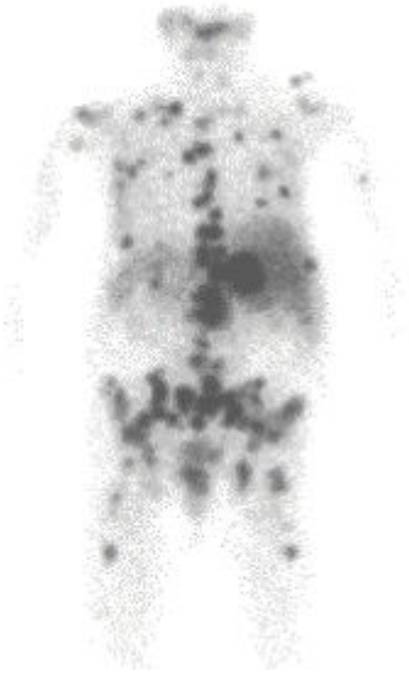
Clinical Study # 4: Patient MR

- 35 Y/O WM
- History of difficult-to-control HTN
- Mass seen on CT
- thyroid blocked with SSKI solution
- injected with 9.8 mCi of I-123 mIBG



Clinical Study # 5: Patient KT

- 60 y/o WF
- History of pheochromocytoma 8 years prior to this study.
- Has recurrence of HTN and other symptoms
- Medication: beta blockers
- thyroid blocked with SSKI solution
- injected with 10 mCi of I-123 mIBG



IMAGING OF NEUROENDOCRINE TUMORS: In-111 Octreotide

PATIENT INDICATIONS

- In-111 Octreotide is indicated for the scintigraphic localization of primary and metastatic neuroendocrine tumors bearing somatostatin receptors.

TUMOR TYPES IMAGED

- Neuroblastomas
- Pheochromocytomas
- Paraganglioma
- Carcinoid Tumors
- Medullary Thyroid Ca
- VIPoma
- Insulinomas
- Gastrinomas
- Pituitary Adenoma
- Glucagonoma
- Islet Cell Carcinomas
- Small Cell Lung Ca

CHARACTERISTICS OF In-111

- t_{phys}= 2.805 d = 67.32 hr
- 171.3 keV gamma: 90.2 % abundance
- 245.4 keV gamma: 94.0 % abundance

RADIOTRACER USED

- 3-6 mCi of high purity In-111 trichloride in dilute HCl in a 10 ml vial

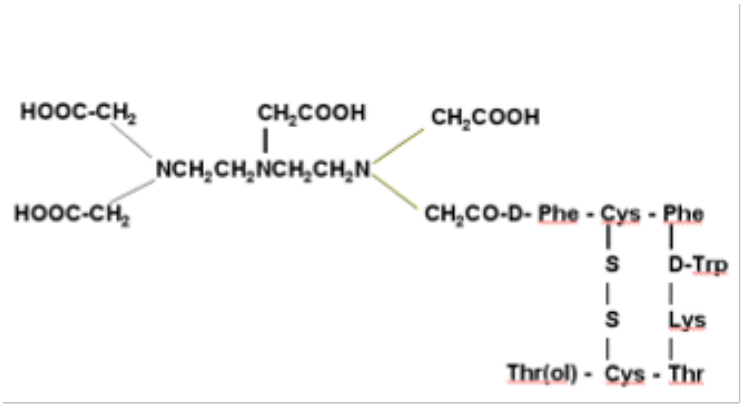
RADIOCHEMICAL REACTION

- In^{3+} + DTPA-Octreotide ----------> In-DTPA-octreotide final pH: 3.8-4.3

BASIC LABELING THEORY

- DTPA group is covalently bonded to Octreotide molecule. In-111 actually bonds to DTPA portion of molecule, not to octreotide

MOLECULAR STRUCTURE OF OCTREOTIDE



PATIENT PREPARATION

- Patient must be very well hydrated before the dose and for up to 48 hr afterward to minimize internal radiation dose
- Patient must take a mild laxative the evening before administration of the drug and continue for 2 days.

ADMINISTERED DOSE

- For Planar/pediatric imaging: 3 mCi = 111 MBq
- For SPECT imaging: 6 mCi = 222 MBq
- Must perform visual inspection to insure absence of particulates

CONTRAINDICATIONS

- Sensitivity to somatostatin and its analogues

ADVERSE REACTIONS OCCURRING IN <1% OF ALL PATIENTS

- dizziness
- fever
- flushing
- headache
- hypotension
- increased liver enzymes
- joint pain
- nausea
- sweating
- weakness

ADVERSE REACTIONS OCCURRING IN <3% OF ALL PATIENTS

- diarrhea and vomiting
- abdominal
- pain/discomfort
- injection site pain

CLINICAL PHARMACOLOGY

- Pentetreotide is a long acting analog of the hormone somatostatin
- Initially concentrates in plasma.
- The In-111 complex binds avidly to somatostatin receptors throughout the body.
- Within 1 hr, most of the In-111 octreotide distributes to extravascular body tissues and in tumors containing a high density of somatostatin receptors.
- After background clearance via the kidneys, visualization of somatostatin rich receptors is achieved.
- $t_{1/2}$ of clearance from blood is 7-8 min
- By 20 hr post injection, <1% of In-111 activity remains in blood.
- Whole body biological half-life of In-111 Octreotide is 6 hr

NORMAL DISTRIBUTION OF In-111-Octreoscan

- Normal pituitary gland
- thyroid gland
- liver
- spleen
- kidneys
- urinary bladder
- bowel (occasionally)

INTERNAL RADIATION DOSIMETRY

ORGAN	RADS / 6 mCi
KIDNEYS	10.8
LIVER	2.4
SPLEEN	14.8
BONE MARROW	0.7
BLADDER WALL	6.1
STOMACH WALL	1.1
UPPER GI	1.2
LOWER GI	1.6
ADRENALS	1.5
THYROID	1.5

CLINICAL IMPACT OF OCTREOSCAN IMAGING

- Yielded information about localizations not previously identified: 27.9% (57/104)
- Demonstrated uptake in lesions known to exist, but not verified as neuroendocrine tumors 28.2% (55/195)
- Localized neuroendocrine tumors in patients with clinical and hormonal evidence of tumor, but no prior localizations 37.5% (21/56)
- Produced a change in patient management-31.1% (64/206)

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