

## EL16. Radiopharmaceutical Diagnosis and Therapy of Sympatho-medullary Disorders

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It is now 17 years since I-131-meta-iodobenzylguanidine (MIBG) was introduced to locate pheochromocytomas (pheo) and 15 years since its therapeutic use. The location of pheo, neuroblastomas (neuro) and paragangliomas with I-131 or I-123-MIBG is now a standard procedure. MIBG has a research role in locating other neuroendocrine tumors, depicting the sympathetic nervous system and treating MIBG-avid tumors. Development of I-131-MIBG has also led to an array of related tracers.

MIBG uptake is a specific, high affinity, saturable, energy and sodium dependent "type 1 uptake" across the cell membrane followed by storage in hormone vesicles. MIBG scintigraphy is thus interfered with by a variety of drugs. Greatest experience has been with I-131-MIBG the dosimetry and imaging of which are suboptimal and which led to use of I-123-MIBG, I-125-MIBG for animal studies, autoradiography and intra-operative probes for tumor localization, positron emitting I-124-MIBG and brominated or fluorinated analogs, C-11-hydroxy-ephedrine and catecholamines for PET. Radiopharmaceutical therapy is delivered by high specific activity I-131 or I-125-MIBG.

Multiple studies show MIBG to be a safe, non-invasive procedure to locate most pheos and paragangliomas, including sporadic, benign, intra-adrenal pheo; sporadic, extra-adrenal pheo; locally

invasive and metastatic lesions; and familial pheo. MIBG has also been shown to be as sensitive and specific for neuro as pheo (Sens 79–91%, Spec 88–99%). This is particularly so for detection of bone marrow involvement. Many neuroendocrine tumors share the APUD property, and are imaged with MIBG but experience is limited and sensitivity not as high.

Uptake of MIBG in heart and salivary glands occurs into presynaptic sympathetic neurons. Reduction occurs in denervation and autonomic neuropathy. Reduction of cardiac tracer uptake also occurs in cardiomyopathy, heart failure, and cardiotoxicity and may be prognostic.

The observation that many metastatic pheo and neuro retained significant I-131-MIBG led to therapy with large activities. No pharmacological toxicity but mild to moderate acute radiation sickness may occur. Myelo-suppression was not seen in adults but occurred in children. Doses are designed to deliver whole body radiation doses of <100–200 rad. Multiple series report significant complete and partial therapeutic responses (reduction in tumor volumes or hormone secretion) in at least a minority of patients (39/127 pheo, 72/255 neuro, 10/51 carcinoid, 6/18 MCT). In 1996 MIBG therapy must be considered an experimental modality which shows promise, but much remains to be learned.