^{123}I-MIBG Imaging: Patient Preparation and Technologist's Role

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The radiopharmaceutical ^{123}I-metaiodobenzylguanidine (MIBG) was approved by the Food and Drug Administration in March 2013 for the assessment of myocardial sympathetic innervation in the evaluation of patients with heart failure and an ejection fraction of no more than 35%. Almost any well-equipped nuclear medicine or nuclear cardiology laboratory can perform this test, although there is a need for special attention to patient preparation, dose calibration, and proper timing of the image acquisition. This article reviews the role of the nuclear medicine technologist and some practical aspects of cardiac sympathetic ^{123}I-MIBG imaging of which the laboratory team needs to be mindful.

Key Words: ^{123}I-MIBG; cardiac sympathetic imaging; cardiac denervation; techniques for MIBG imaging

The radiopharmaceutical ^{123}I-metaiodobenzylguanidine (MIBG) (AdreView; GE Healthcare) was approved by the Food and Drug Administration in March 2013 for the assessment of myocardial sympathetic innervation in patients with New York Heart Association class 2 or 3 heart failure and an ejection fraction of less than 35% (*1*). The role of this test in clinical practice is currently evolving. This article outlines the practicalities of the use of ^{123}I-MIBG.

The use of ^{123}I-MIBG can be best demonstrated by a case presentation. A 65-y-old man presents with mild limitations due to shortness of breath on exertion. He had a heart attack 2 y previously and has been somewhat limited ever since. A recent myocardial perfusion imaging test showed left ventricular scarring but no ischemia and a left ventricular ejection fraction of 36%. However, a recent echocardiogram

obtained during a hospitalization at another facility showed an ejection fraction of 33%. The patient is advised to consider an implantable cardioverter defibrillator but is reluctant because a relative has an implantable cardioverter defibrillator that frequently fires inappropriately.

It is certainly clear that implantable cardioverter defibrillators save lives; their prophylactic implantation in patients who have known heart failure with low ejection fractions is considered standard therapy (*2*). However, these devices are sometimes associated with complications and are expensive, and many are implanted for each life saved (*3,4*).

For patients such as this one, who have borderline indications for implantable cardioverter defibrillators and are reluctant to proceed, physicians have a few options: accept that the patient does not want the device; try to convince the patient to have the device implanted; define the ejection fraction more exactly via another diagnostic medical imaging modality; or perform cardiac sympathetic imaging with ^{123}I-MIBG for risk stratification. The heart-to-mediastinum ratio provided by ^{123}I-MIBG imaging is a powerful prognostic indicator in these patients, and such information may be useful in shared decision making by physicians and patients (*5–8*).

EQUIPMENT PREPARATION

To properly acquire ^{123}I-MIBG images, the camera must allow for frontal planar imaging. Anterior frontal plane images are a requirement, whereas SPECT images are optional but are usually obtained. The nuclear cardiology system should have low-energy, high-resolution collimation, and the camera should be able to obtain specific sequences from the imaging protocol, for example, static and SPECT imaging. Setting up and testing the imaging sequence before the day of dosing is often helpful and recommended.

The dose calibrator should also be inspected before the study is ordered. The dose calibrator should have a ^{123}I-specific setting, and a correction factor specific for the laboratory's instrument must be obtained. It is strongly recommended that a commercial copper sleeve or copper tube be used during dose calibration to lessen scatter counts from low-energy photons, which can give falsely low readings for ^{123}I-MIBG (*9*).
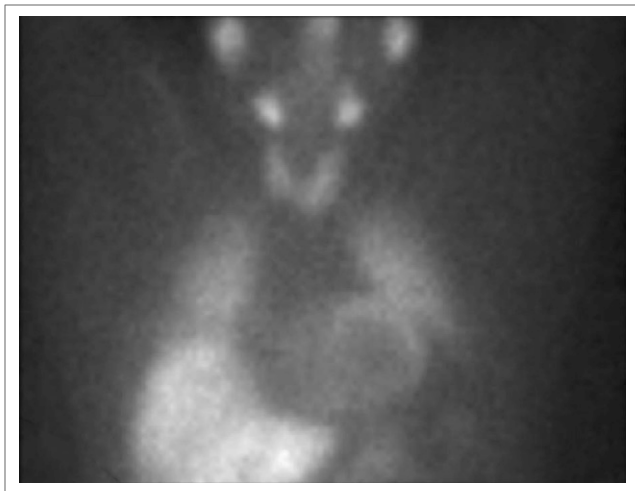
FIGURE 1. Anterior view of ^{123}I-MIBG 3 h 50 min after injection.

Two static anterior planar acquisitions are obtained when imaging with ^{123}I-MIBG (at 15 min and 3 h 50 min after injection). With a dual-head camera, the detectors should be positioned in the anterior and left lateral positions. The anterior field of view (FOV) will be focused on acquiring the myocardium and the mediastinal region for later processing (Fig. 1). The organs of interest should be positioned in the center of the field of view, with the apex of both lungs kept close to the top central field of view and the base of the myocardium kept in the bottom of the central field of view.

A 10-min anterior acquisition in a $128 \times 128 \times 16$ matrix allows for adequate counting statistics. Photon acquisition should be centered on a 159-keV peak with a 20% window.

PATIENT PREPARATION

When a clinical laboratory is preparing a patient for cardiac ^{123}I-MIBG imaging, most of the steps typical of nuclear cardiology imaging are followed. The imaging team should be mindful of the patient's past medical history, including allergies, medications, and the general health history. There are also some medical issues particular to ^{123}I-MIBG imaging. ^{123}I-MIBG is contraindicated in patients with known hypersensitivity to iobenguane or iobenguane sulfate; however, it is also customary to screen potential patients for allergies to iodine-containing materials by asking if they have had any prior reactions to iodinated contrast material, shellfish, strawberries, or cranberries.

Particular attention must be paid to medication history. Table 1 provides a list of medications that affect ^{123}I-MIBG imaging. This list includes medicines that the patient may not record unless specifically queried, such as over-the-counter cold medicines and cocaine. Certain common cardiac medications, including labetalol and calcium channel antagonists, also need to be stopped temporarily before ^{123}I-MIBG imaging.

TABLE 1
Medications That Affect ^{123}I-MIBG Imaging (*13*)

Drug or class	Examples	Mechanism of interference (known or expected)	Discontinuation before ^{123}I-MIBG scan (d)
Opioid		Uptake inhibition	7–14
Cocaine		Uptake inhibition	7–14
Tramadol		Uptake inhibition	7–14
Tricyclic antidepressants	Amitriptyline and derivatives, imipramine and derivatives, amoxapine, doxepin, others	Uptake inhibition	7–21
Sympathicomimetics*	Phenylpropanolamine, ephedrine, pseudoephedrine, phenylephrine, amphetamine, dopamine, isoproterenol, salbutamol, terbutaline, fenoterol, xylometazoline	Depletion of granules	7–14
Antihypertensive or cardiovascular agents	Labetalol	Inhibition of uptake and depletion	21
	Reserpine	Depletion and transport inhibition	14
	Bretylium, guanethidine	Depletion and transport inhibition	14
	Calcium channel blockers (nifedipine, nicardipine, amlodipine)	Increased uptake and retention	14
Antipsychotics	Phenothiazines[†] (chlorpromazine, promethazine, fluphenazine, others)	Uptake inhibition	21–28
	Thioxanthenes (maprotiline, trazodone)	Uptake inhibition	21–28
	Butyrophenones (droperidol, haloperidol)	Uptake inhibition	21–28
	Loxapine	Uptake inhibition	7–21

*Components of bronchodilators, decongestants, and diet aids.
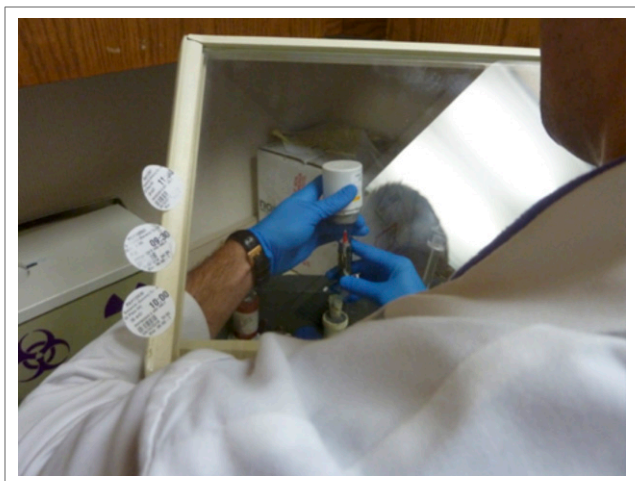[†]Frequent components of antiemetic and antiallergic agents.

FIGURE 2. Proper technique for drawing a ^{123}I-MIBG dose.

Two particularly relevant medical conditions include Parkinson disease and kidney disease. Patients with Parkinson disease have impaired cardiac uptake of ^{123}I-MIBG (*10*). Renal insufficiency is considered a relative contraindication for ^{123}I-MIBG testing since the radiopharmaceutical is cleared by the kidneys, although a recent report called into question this conventional position (*11*).

Patients who have an increased risk for thyroid cancer should be considered for potassium iodide pretreatment in order to block thyroid uptake and to lower the radiation dose to the thyroid (*1,12*). Patients at increased risk would presumably include young patients and those with a personal or family history of thyroid cancer. Potassium iodine was not routinely administered before ^{123}I-MIBG in the pivotal ADMIRE-HF trial (*5*).

Patients should be informed of key elements of the ^{123}I-MIBG test beforehand to help alleviate their uncertainty and apprehension. Nuclear medicine tests can sound frightening to some people, so it is important to outline the procedure, time requirements, and reasons for the test. Patients are generally instructed to be well hydrated before the test, but care should be taken with heart failure patients who are on fluid restriction.

Radiation dosimetry should also be mentioned to the patient. The effective dose for an adult is 5.07 mSv for the injection of 370 MBq (10 mCi) of ^{123}I (13.7 μSv/MBq × 370 MBq, or 0.507 mSv/mCi × 10 mCi) (*1*). There is also a small amount of radiation exposure from attenuation correction. The total exposure is relatively low compared with other procedures in nuclear cardiology and is comparable to about 15 mo of average background radiation.

The cost and logistics of this radiopharmaceutical cause the no-show policy to be more important than usual. ^{123}I-MIBG is a particularly expensive radiopharmaceutical, and the dose travels a long distance before administration. Health insurance companies, including the Centers for Medicare and Medicaid Services, allow nuclear cardiology facilities to bill patients for

no-shows, but the laboratory must have a written policy in place and it is good practice to have patients acknowledge the policy in writing.

RADIOPHARMACEUTICAL PREPARATION

The dose of ^{123}I-MIBG is calibrated to be 370 MBq (10 mCi) at 12:00 PM on the day of administration. The dose arrives in a single-use vial containing 5 mL of ^{123}I-MIBG (74 MBq/mL, or 2 mCi/mL). The radiopharmaceutical expires 36 h after the calibration time and should be stored at between 68°F and 77°F, following hospital safety protocols.

Using aseptic technique and proper radiation safety, the technologist should draw 370 MBq (10 mCi) into a shielded syringe (Fig. 2). The syringe should be placed into the dose calibrator to verify the proper number of megabecquerels (or millicuries) before injection. The dose can then be administered to the patient via a large peripheral vein over 1–2 min. The intravenous line should be flushed with saline before isotope injection to verify proper venous access and again after injection to remove any accumulated residual activity. During the timed administration, the patient should be continually monitored for any hypersensitivity or other reactions to the medication, such as itching, burning, or tingling sensations at the injection site. A postinjection assay is performed on the syringe to determine residual radioactivity and the total activity administered to the patient.

THE ^{123}I-MIBG ACQUISITION

Because of the short injection-to-scan time, the technologist should ensure that the camera is unoccupied before administering the pharmaceutical. Preparing the acquisition setup before injection is also helpful.

Exact timing of the acquisition is important; a stopwatch should be used. An early 10-min anterior planar image is obtained starting at 15 min after injection, and a late 10-min anterior planar image is obtained starting at 3 h 50 min after injection. These combined images
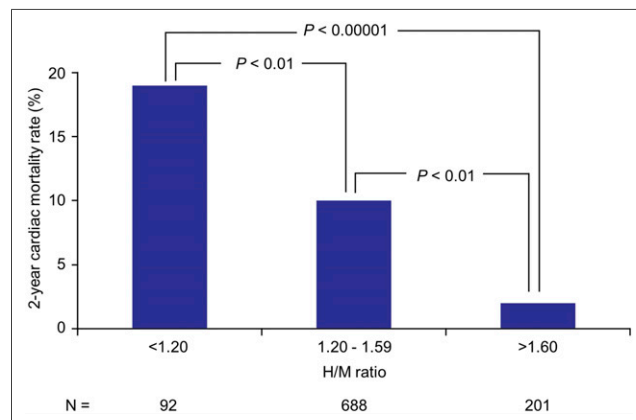

FIGURE 3. Association of cardiac death with heart-to-mediastinum (H/M) ratio.
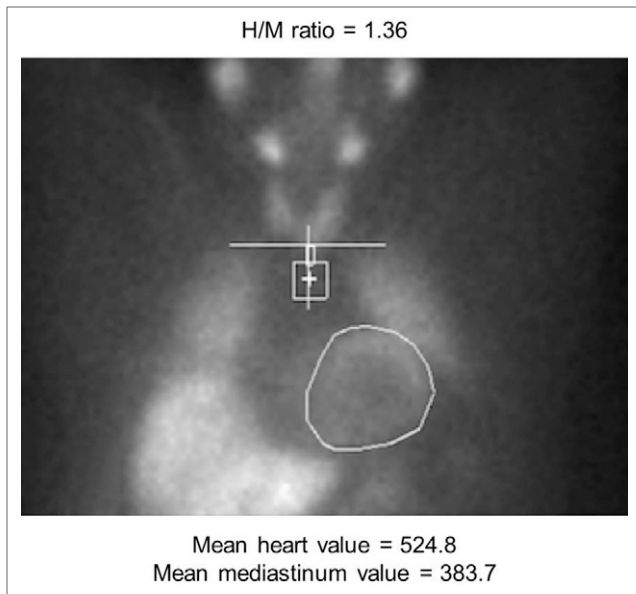
FIGURE 4. Heart-to-mediastinum (H/M) ratio obtained with ^{123}I-MIBG.

H/M ratio = 1.36

Mean heart value = 524.8
Mean mediastinum value = 383.7

allow for calculation of the washout ratio of the isotope (*1*).

Between these acquisitions, patients are allowed to eat and are encouraged to stay well hydrated but not excessively so if they have heart failure. Patients should also be advised that they are radioactive and to avoid small children and going through some airport security systems. SPECT images are acquired after the late planar acquisition.

The primary prognostic parameter supplied by ^{123}I-MIBG imaging is the heart-to-mediastinum ratio on the delayed images, which has been shown to predict the 2-y cardiac mortality rate (Fig. 3) (*5*). The regions of interest must be drawn around the heart and in the mediastinum in the prescribed fashion according to the product package insert. In brief, an irregular region of interest is drawn around the whole heart, defining the epicardial border. The number of counts and pixels in the region of interest

are recorded. For the mediastinal region of interest, a horizontal line is drawn at the apices of the lungs. A vertical line is then drawn about equidistant between the right and left lungs. At the intersection of the horizontal and vertical lines, counts 15 pixels and below are marked. Starting with the fourth pixel below the intersection, the area with the lowest counts is identified and, if there are multiple areas, the most superior selected. At the lowest pixel, a 7×7 pixel region of interest is drawn, and the number of counts in this 49-pixel region of interest is recorded. The heart-to-mediastinum ratio is equal to the counts per pixel in the cardiac region of interest divided by the counts per pixel in the mediastinal region of interest (Fig. 4).

THE SPECT ACQUISITION

The 4-h SPECT image dataset allows the clinician to visualize myocardial uptake and retention of ^{123}I-MIBG in the classic short-, vertical-, and horizontal long-axis views. Our laboratory uses a circular orbit with 180° of acquisition, and we acquire 64 projections using 32 stops of approximately 25 s/stop. An attenuation correction map is acquired simultaneously. The study is acquired in a $64 \times 64 \times 16$ matrix and is nongated.

IMAGE PROCESSING

Sample anterior planar images are shown in Figure 5. We customarily display the planar images in a 2-view panel (one image displaying the raw image and the other displaying the heart-to-mediastinum ratio along with the regions of interest).

The SPECT reconstruction parameters may vary depending on the site-specific routine, and the technologist should consistently use the reconstruction parameters best suiting the laboratory. The ^{123}I-MIBG images are reconstructed in a manner similar to that of myocardial perfusion SPECT images. Either standard filtered backprojection or iterative reconstruction can be used. Typically, a low-pass filter is used, with a cutoff of 0.50 and an order of 5.00. The images are then displayed in a fashion similar to that of SPECT
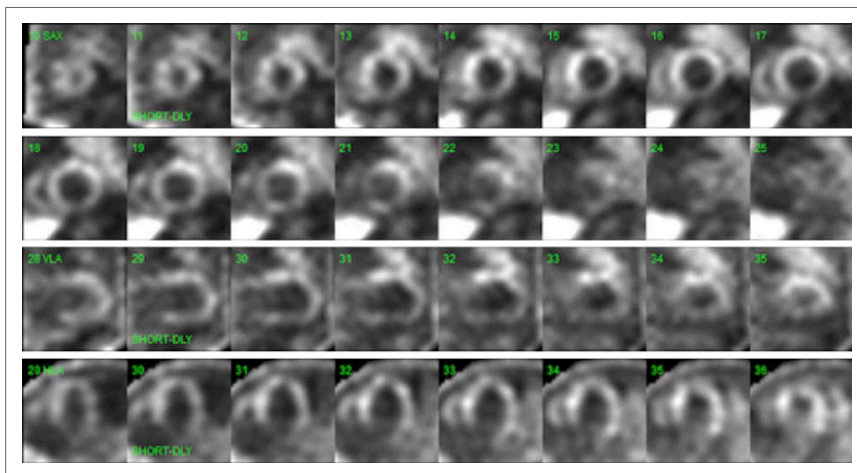

FIGURE 5. Classic SPECT myocardial display of ^{123}I-MIBG images after reconstruction.

myocardial perfusion images. Creating reconstruction defaults can help to standardize methods.

In 2010 Flotats et al. proposed standardization of ^{123}I-MIBG cardiac sympathetic imaging on behalf of the European Association of Nuclear Medicine Cardiovascular Committee and the European Council of Nuclear Cardiology (13). Their publication provides more details about the acquisition and reporting of ^{123}I-MIBG imaging.

CONCLUSION

Cardiac sympathetic ^{123}I-MIBG imaging can be performed by almost all well-equipped nuclear medicine and nuclear cardiology laboratories. The procedure requires special attention to patient preparation, dose calibration, and timing of image acquisition. As opportunities to use this technique grow, its exact clinical role should become clear. The test is expected to provide clinicians with useful prognostic information about cardiovascular risk in patients with heart failure.

DISCLOSURE

No potential conflict of interest relevant to this article was reported.

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