Classification and Definition of Cardiomyopathies (WHO/ISFC, 1996)

- Dilated Cardiomyopathy (DCM)
- Hypertrophic Cardiomyopathy (HCM)
- Restrictive Cardiomyopathy (RCM)
- Arrhythmogenic RV Cardiomyopathy
- Unclassified Cardiomyopathies
- Specific Cardiomyopathies
  - ischemic, valvular, hypertensive, inflammatory, metabolic, general system disease, connective tissue disorder, infiltrations, granulomas, muscular dystrophies, neuromuscular disorders, sensitivity and toxic reactions, peripartum

Nuclear Cardiology in Cardiomyopathies

- Cardiac pump function
  - MUGA (Tc-99m HSA/RBC)
  - Gated SPECT (Tc-99m mibi/tetrofosmin, thallium-201)
- Myocardial function
  - Perfusion (Tl-201, Tc-99m mibi/tetrofosmin)
  - Metabolic (I-123-BMIPP, F-18 FDG PET)
  - Inflammation (Tc-99m PYP, Ga-67 citrate, etc)
  - Neurotransmitter (I-123 MIBG)
  - Molecular (Tc-99m annexin V)

Role of Imaging In Cardiomyopathies

- Prognosis in heart failure
- Risk stratification of patients with heart failure
- Selecting patients who will benefit most from aggressive treatment options (e.g. revascularization, ICD, biventricular pacing, transplantation, LVAD etc.)
Introduction

- LV dysfunction is very commonly seen in the clinical setting & can result from a variety of insults to the myocardium
- Ischemic Cardiomyopathy is by far the commonest, accounting for most of the morbidity & mortality associated with poor LV function

Imaging In Cardiomyopathies

- Radionuclide Angiography (RNA)
- SPECT Perfusion Imaging
- MIBG Receptor Imaging
- PET Imaging
- Echocardiography
- Multi-Slice CT
- Cardiac MRI

Ischemic Cardiomyopathy

- Ischemic cardiomyopathy associated with depressed LV function represent a very common management problem.
- Overwhelming evidence that such patients have poor prognosis when treated medically, and long-term benefits of revascularization (PTCA, CABG) are far superior. (CASS Registry)
- Increased operative morbidity & mortality in these patients make the correct selection of patients for revascularization crucial.
- Identifying viable myocardium from non-viable tissue is of utmost importance as it is well known that revascularization in patients with substantial viable myocardium can improve LV function, symptoms and survival.

Definition of Viability

- Dysfunctional myocardium in this group of patients can result from the following mechanisms:
  - Necrosis / Fibrosis (Scar)
  - Chronic ischemia without necrosis (Hibernation)
  - Transient ischemia despite reperfusion (Stunning)
- Both hibernation and stunning represent viable myocardium, and nuclear imaging can accurately identify viable from infarcted myocardium
Information obtained from Gated Myocardial Perfusion SPECT

- **Perfusion**
  - Ischaemia
  - Infarction

- **Function**
  - Global LVEF
  - LV volumes
  - Diastolic function
  - Regional function

**Implements:**
- Diagnosis of CAD
- Specificity
- Sensitivity
- Prognosis of CAD
- Viability assessment
- Pre-operative risk assessment

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**Dobutamine GSPECT Viability Assessment**

- Recognized but not widely used method of viability assessment, akin to low dose dobutamine ECHO
  - Yamagushi et al. J Nucl Cardiol 1999;6:626 (FDG)
  - Leocini et al. J Nucl Cardiol 2001;7:426
  - Iskandrian et al. JACC 2002
  - Tamaki et al. JNM 2001

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Exercise
- Stress - rest
- Sestamibi SPECT

Rest gated Sestamibi SPECT

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**Exercise Stress - rest Sestamibi SPECT**
Heart failure is a problem of increasing importance in cardiovascular medicine, and may result from various insults:
- Ischemic cardiomyopathy
- Toxic (e.g. anthracycline) cardiomyopathy
- Hypertrophic cardiomyopathy (HCM)
- Viral Myocarditis/Cardiomyopathy
- Arrhythmogenic RV Dysplasia (ARVD)
- Childhood dilated cardiomyopathy
- Others (idiopathic, post partum etc.)

Sympathetic stimulation is one of the main compensatory mechanisms in the failing heart.
As heart failure progresses, cardiac stores of nor-epinephrine are depleted but circulating nor-epinephrine concentration is elevated.
This effect has been directly related to degree of left ventricular dysfunction and risk of death.
Cardiac Innervation

The failing heart is characterized not only by a decrease in the catecholamine content in the myocytes and impairment of nor-epinephrine release and uptake but also by abnormalities of cardiac nerve terminals, including reduced uptake of nor-epinephrine.

Cardiac Innervation Imaging

With the introduction of catecholamine analogues, e.g., $^{123}$I MIBG ($^{99m}$Tc MIBG), noninvasive assessment of pre-synaptic neuronal function has become possible in the clinical setting.

New radiopharmaceuticals such as labeled $^{18}$F-fluorometaraminol are being developed to demonstrate the integrity of cardiac sympathetic nerves with better spatial resolution.

MIBG & THE MYOCARDIUM

- Iodine-123-Metaiodobenzylguanidine (MIBG)
  - CATECHOLAMINE RECEPTOR SEEKER
  - Noradrenaline analogue


- Uptake directly proportional to the quantity of active adrenergic receptors

- Cardiac image reflect the distribution of receptors in the myocardium

Nor-epinephrine uptake
MIBG IMAGING IN CARDIAC FAILURE - CONCEPT

- **CARDIAC FAILURE**
  - Depletion of norepinephrine stores
  - Desensitization of adrenoreceptors
  - Functional autonomic imbalance in the myocardium

- **MIBG UPTAKE DEPENDENT ON THE CATECHOLAMINE STORES**
- **REDUCTION IN UPTAKE IS OF PROGNOSTIC SIGNIFICANCE**

MIBG Uptake in Heart Failure

- Decreased cardiac uptake
- Increased MIBG clearance
- Increased lung uptake
- Heterogeneity of MIBG distribution
- Correlated with cardiac dysfunction and prognosis
MIBG Delayed (4hr) Planar Image

- Advanced Baseline: Impairment of cardiac sympathetic nerve function
- Mild impairment of cardiac sympathetic nerve function

MIBG Delayed (4hr) Planar Image

- Before Treatment
- After Treatment

Polar Quantitation of SPECT MIBG images

- Abnormal
- Normal

Serial MIBG Scans

- Survivor
- Non-survivor

Mitsui Circ J 2002;66:537-543
Prognostic Significance of Serial MIBG Scans

Sites of infarcts and perfusion defects determined by sestamibi SPECT correlate well with I-123 MIBG images, but areas of reduced MIBG uptake are larger than the infarct size, and correlate qualitatively with ischemic-infarcted areas, suggesting that imaging neuronal ischemia is a highly sensitive imaging technique.

Prognostic Significance of Serial MIBG Scans

Clinical Results: Congestive Heart Failure

- Medications such as beta blockers and angiotensin converting enzyme inhibitors improve morbidity and mortality in patients with congestive heart failure.
- MIBG studies show improvement of sympathetic nerve dysfunction in heart failure after long term therapy with angiotensin converting enzyme inhibitors.
- Possible role for MIBG imaging to monitor the effect of pharmacological therapy.
Abnormal MIBG uptake occurs in patients with ventricular tachycardia, even in the absence of CAD.

- MIBG uptake was reduced in 85% of the patients with arrhythmogenic right ventricular dysplasia (ARVD) and normal myocardial perfusion studies.

The location of defects on the MIBG scintigraphy correlated well with site of origin of VT determined by invasive electrophysiologic studies.

- The presence of denervated but viable myocardium may have important implications for the pathogenesis of ventricular arrhythmias.

Potential utility of MIBG imaging for noninvasive detection of localized sympathetic denervation is currently under investigation.

- Aim: selection patients in need of implantable defibrillators (AICD).

Arrhythmogenic heart disease:

- 123-I MIBG
- 99m-Tc-MIBI
Arrhythmogenic RV Dysplasia

PET $^{11}$C-HED

Childhood Dilated Cardiomyopathy

- In children with idiopathic dilated cardiomyopathy cardiac adrenergic neuronal function is impaired as documented by significantly decreased heart to mediastinal uptake ratio.
- MIBG scintigraphy has been proposed as a key method for evaluation of the disease and an important factor in considering heart transplantation.

Toxic Cardiomyopathy
(e.g. Anthracycline)

- Anthracycline chemotherapeutic agents such as doxorubicin are known to cause cardiotoxicity in a dose dependent fashion, which often limit their use.
- Usual assessment is by serial MUGA scans to look for deterioration of function.
- Abnormal cardiac adrenergic neuronal activity (decreased MIBG uptake in the heart) showed more linear dose dependent deterioration than LVEF suggesting potential utility of MIBG as a sensitive marker of cardiac damage.

Viral Myocarditis

- Variety of viruses can cause myocarditis and cardiomyopathy in susceptible hosts
- Myocardial damage can be assessed by anti-myosin or PYP imaging
- Lack of MIBG uptake and increased washout also seen, and is of prognostic significance
**Myocardial Hypertrophy**

- In myocardial hypertrophy secondary to mechanical overload, such as valvular aortic stenosis, essential hypertension, and pulmonary arterial hypertension, MIBG uptake is reduced and washout increased.
- After medical treatment MIBG uptake was improved indicating that such presynaptic abnormalities, typical for failing hearts, may be reversible.

**Hypertrophic Cardiomyopathy I**

- Genetic disease when there is asymmetric hypertrophy of the septum, apex etc
- May lead to LVOT obstruction and also depressed LVEF
- Nuclear imaging may be useful
- Echo usually clinches the diagnosis
- MRI a better tool for imaging
- MIBG also show depressed uptake in these subjects, and can be used to monitor response to treatment

**Hypertrophic Cardiomyopathy II**

- Perfusion Imaging may demonstrate asymmetrically thickened septum, apex etc
- Fixed or even reversible defects in the absence of epicardial coronary disease
- Radionuclide Angiography:
  - Hyperdynamic LV systolic function
  - Impaired diastolic filling
  - Disproportionate upper septal thickening
- Poor Prognostic Signs
  - Depressed LV systolic function
  - Dilated LV
  - Fixed perfusion defects
  - Reversible defects – at risk of arrhythmias and sudden death
Others

- MIBG imaging has shown interesting results in:
  - in myocardial infarction,
  - re-innervation after myocardial infarction,
  - other forms of ischemic heart disease,
  - diabetes mellitus,
  - re-innervation after heart transplantation.

Cardiac Sarcoidosis

- Rare but frequently fatal cause of cardiomyopathy, often undiagnosed
- Several non invasive diagnostic procedures available:
  - Myocardial Biopsy (1/3 positive)
  - MRI (gadolinium-enhanced)
  - ^{67}\text{Ga} \text{Gallium imaging}
  - Thallium SPECT (reverse distribution)
  - ^{123}\text{I} \text{BMIPP imaging}
  - Fasting ^{18}\text{FDG PET}
  - Echocardiography

Cardiac Sarcoidosis

- Nuclear imaging useful in monitoring progress in treatment of sarcoid, e.g. after steroid therapy
Cardiac resynchronization therapy (CRT) is a new, proven treatment for selected patients with heart failure-induced conduction disturbances and ventricular dis-synchrony. When used in combination with stable, optimal medical therapy, CRT can reduce symptoms by restoring the mechanical sequence of ventricular activation.

Ventricular dis-synchrony has several important consequences that adversely affect cardiac performance:
- Abnormal interventricular septal wall motion
- Reduced diastolic filling time
- Prolonged mitral regurgitation duration
- Reduced dP/dt

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Nuclear Cardiology

Heart Failure and Ventricular Dysynchrony

Many patients with advanced systolic heart failure exhibit significant intra- or interventricular conduction delays (IVCD) that disturb the synchronous beating of the ventricles so that they pump less efficiently. This delayed ventricular activation and contraction is referred to as ventricular dysynchrony and is recognized by a wide QRS complex on ECG. Typically, the IVCD has a left bundle branch block (LBBB) morphology.

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Role of Nuclear Cardiology in Cardiac Resynchronization

- Nuclear imaging can help in determining which patients will benefit from such intervention, as it has been shown that patients without significant viability do not show improvement in LVEF & volumes post CRT (Sciagra et al. JNM 2004,45:2)
- Nuclear imaging can also characterize the before & after effects of CRT by phase imaging, and also the changes in EF and volumes after CRT (Tsurugaya et al. Am J Cardiol 2004,94:1)
Role of Nuclear Imaging in LVAD assessment

- Left Ventricular Assist Devices are being increasingly used as a bridge to cardiac transplantation, recovery of LV dysfunction or as a semi-permanent device.
- Gated Blood Pool Imaging (MUGA) can assist in the assessment of both the LV and RV function, with or without LVAD augmentation.
- Assessment of RV function is integral in the decision to wean the device.

Nuclear Imaging in Stem Cell Transplantation

- Myocardial stem cell therapy a new & novel treatment in end-stage heart disease when all other therapies have failed.
- Both metabolic & perfusion can be used to track improvement in both parameters, together with changes in EF post transplantation.
Myocardial Non-Compaction

- A rare familial cause of CCF
- Often unrecognized, diagnosis usually by Echocardiography
- Nuclear perfusion and innervation imaging may be useful in showing reduced perfusion and de-innervation in areas of non-compaction

Conclusions I

- Myocardial neurotransmitter imaging has been successful in assessing cardiac autonomic innervation in various cardiomyopathies, and can be used as a prognostic indicator
- Early detection of abnormalities before evidence of structural changes is an important goal for MIBG scintigraphy
- Monitoring of medical therapeutic procedures also seems to be a promising application of neurotransmitter imaging
Conclusions II

- Nuclear imaging is thus vital to the diagnosis & treatment of various forms of cardiomyopathy
- Perfusion, metabolic & innervation imaging are the mainstay of imaging formats in evaluating patients with heart failure symptoms, together with EF determination, so that the most appropriate treatment strategies can be applied