Cardiac radionuclide imaging has wide applications such as diagnosis, disease severity assessment, decisions regarding treatment strategies, evaluation of treatment effects, and prognosis of cardiac diseases. The aim of these guidelines is the effective and efficient use of cardiac radionuclide imaging in the diagnosis of cardiac diseases. To that end, we have summarized the usefulness and evidence levels of diagnostic test techniques on the basis of previous reports. The characteristics and usefulness of each diagnostic test technique are outlined in the first half of the guidelines, and the use of radionuclide imaging in specific cardiac diseases and pathologies is addressed in the second half.

### 2. Basic Principles

This working groups discussed the appropriate use of nuclear cardiology in the clinical setting based on previous reference to the Report of the Committee on Diagnostic Criteria for the Diagnosis of Cardiac Diseases with Nuclear Medicine Techniques (1989–1991, Fukuzaki et al.) and the Standardization of Clinical Indication of New Radiopharmaceutical Agents for Circulatory Organs (1998, Sugishita et al.). Whereas the guidelines for cardiac radionuclide imaging were published by the American Heart Association (AHA), American College of Cardiology (ACC) and American Society of Nuclear Cardiology (ASNC) in 2003, the guidelines for cardiac radionuclide imaging in Japan were proposed on the basis of a detailed review of reports published in Japan in addition to reports from Europe and the United States. The working groups revised the guidelines published in fiscal year 2005 to incorporate new knowledge in the area of nuclear cardiology from the subsequent five years. To provide researchers with the latest reports in the literature, related research papers published in English were retrieved through a computer search. As a result, we cited over 1,000 research papers for this revised guidelines. We decided a literature searching period for each imaging technique on a case by case basis. After a detailed review of selected papers, we...
Table 1. Classification of Recommendations and Level of Evidence

(1) Classification of recommendations

1) Class I
   Conditions for which there is evidence and/or general agreement that a given test is useful and effective

2) Class II
   Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness of a test
   Class IIa
   Weight of evidence/opinion is in favor of usefulness
   Class IIb
   Weight of evidence/opinion is less established based on evidence or opinion

3) Class III
   Conditions for which there is evidence and/or general agreement that the test is not useful and in some cases may be harmful

(2) Level of evidence

1) Level A
   Verified by two or more multicenter randomized intervention trials on 400 or more patients or by meta-analysis

2) Level B
   Verified by two or more multicenter randomized intervention trials on fewer than 400 patients, well-designed comparative studies, or large-scale cohort studies

3) Level C
   Consensus opinion of specialists

3. Imaging Techniques

Imaging techniques were categorized in accordance with radiopharmaceutical agents used in radionuclide imaging. We added new sections such as electrocardiogram (ECG) gating, positron emission tomography (PET), and image fusion techniques to these updated guidelines. We also addressed the classification of the uses of radionuclide imaging in stress tests and in pediatric cases. Myocardial perfusion imaging techniques were categorized into Tl-201-labeled and Tc-99m labeled myocardial perfusion imaging techniques. In addition, myocardial sympathetic nerve imaging using I-123-metaiodobenzylguanidine (I-123 MIBG), myocardial fatty acid metabolism imaging using I-123-beta-methyl-p-iodophenylpentadecanoic acid (I-123 BMIPP), Ga-67 citrate and Tc-99m pyrophosphate imaging were also addressed.

4. Selection of Diagnostic Test Techniques Depending on Pathologies and Diseases

These guidelines address the selection of diagnostic test techniques in acute coronary syndrome (ACS), chronic coronary artery diseases, heart failure, and myocardial viability assessment.

II Practical Guidelines: Imaging Techniques

1. Myocardial Perfusion Imaging

Myocardial perfusion imaging has been established as a major diagnostic technique in nuclear cardiology. It enables the simple and noninvasive assessment of myocardial ischemia and reduction of coronary flow reserve using exercise or pharmacological stress. Myocardial perfusion imaging provides functional information on coronary arteries, which is different from the morphological information provided by coronary angiography. Moreover, it is suitable for the quantitative evaluation of myocardial perfusion conditions. ECG gated single-photon emission computed tomography (SPECT) provides information on myocardial perfusion and left ventricular (LV) function. It is widely used for coronary artery disease detection in clinical practice including the diagnosis of myocardial ischemia and infarction, assessment of severity, assessment of myocardial viability, determination of indication of a revascularization procedure, and assessment of treatment effects. It is also used for assessment of pathologies and to determine the severity of heart failure and cardiomyopathy. Moreover, there is a large amount of data supporting the usefulness of this technique.
Recommendations for myocardial perfusion imaging are listed above (Table 2).

2. Myocardial Sympathetic Nerve Imaging Using I-123 MIBG

I-123 MIBG reflects the distribution of cardiac sympathetic nerve terminals. Thus, using I-123 MIBG it is possible to detect local denervation. The clearance of I-123 MIBG from the heart reflects sympathetic nerve activity. Thus, an increase in rate of clearance is associated with increasing sympathetic nerve activity due to heart failure.

When considering the assessment of prognosis in patients with heart failure, most previous studies have focused on dilated cardiomyopathy.18–19 However, it has been reported that I-123 MIBG imaging is also useful for assessment of prognosis in patients with heart failure associated with ischemic heart diseases.20 It should be noted that in patients with diabetes, decrease in I-123 MIBG accumulated uptake in the LV inferior wall can be observed even in the absence of cardiac disease.21

Recommendations for myocardial sympathetic nerve imaging are as follows (Table 3).

3. Myocardial Fatty Acid Metabolism Imaging Using I-123 BMIPP

This technique is useful for the diagnosis of unstable angina and is highly useful for the diagnosis of early phase of ACS.22 It is also useful for the detection of ischemic myocardial damage (i.e. ischemic memory imaging) in patients with difficulty undergoing stress tests.23 I-123 BMIPP may be useful in the diagnosis of coronary vasospastic angina.24 Differences in myocardial blood perfusion and I-123 BMIPP uptake are sometimes observed in stunned25 and hibernating myocardium.26 Thus, this technique is useful in assessing the pathology of myocardial ischemia.27 I-123 BMIPP may be useful for predicting cardiovascular events.28

Recommendations for myocardial fatty acid metabolism imaging are as follows (Table 4).

4. Inflammation Imaging Using Ga-67 Citrate

Ga-67 citrate is used for the assessment of myocardial lesions in patients with cardiac sarcoidosis and for the auxiliary diagnosis of myocarditis and infective endocarditis.1

5. Cardiac Radionuclide Angiography

Cardiac radionuclide angiography (RNA) is widely used as a highly accurate method of assessing cardiac function.29 Recently, with improvements in the accuracy and technology of echocardiography and the spread of ECG gated SPECT, the use of cardiac RNA has decreased in Japan. However, cardiac RNA at rest is widely applied in the United States for the detection of cardiac toxicity during chemotherapy.30 Cardiac RNA should be more widely used in Japan, particularly in the above clinical setting.

Recommendations for cardiac RNA are listed above (Table 5).

6. Positron Emission Tomography

The usefulness of cardiac PET has been established for diagnosis of myocardial viability using 18F fluorodeoxyglucose (F-18 FDG)31 and the diagnosis of coronary artery diseases using myocardial perfusion imaging.31–33 Rubidium-82 and N-13 ammonia are used in clinical practice in North America.34 Moreover, there has recently been accumulation of evidence for the usefulness of stress myocardial perfusion PET in the prognosis of cardiovascular events.35

**Table 2. Recommendations for Myocardial Perfusion Imaging**

<table>
<thead>
<tr>
<th>Indications</th>
<th>(1)</th>
<th>(2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myocardial perfusion imaging in coronary artery disease</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Diagnosis of myocardial ischemia using stress myocardial perfusion imaging</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Determination of infarct region</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Determination of myocardial viability</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Prognosis assessment and risk stratification</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Determination of treatment effects</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Diagnosis of coronary artery disease in patients with chest pain</td>
<td>Ila</td>
<td>C</td>
</tr>
</tbody>
</table>


**Table 3. Recommendations for Myocardial Sympathetic Nerve Imaging Using I-123 MIBG**

<table>
<thead>
<tr>
<th>Indications</th>
<th>(1)</th>
<th>(2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assessment of severity and prognosis of heart failure</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Assessment of treatment effects of heart failure</td>
<td>Ila</td>
<td>C</td>
</tr>
<tr>
<td>Arrhythmogenic disease</td>
<td>Iib</td>
<td>C</td>
</tr>
</tbody>
</table>


**Table 4. Recommendations for Myocardial Fatty Acid Metabolism Imaging Using I-123 BMIPP**

<table>
<thead>
<tr>
<th>Indications</th>
<th>(1)</th>
<th>(2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis of unstable angina</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Diagnosis of coronary vasospastic angina</td>
<td>Ila</td>
<td>C</td>
</tr>
<tr>
<td>Diagnosis of acute myocardial infarction</td>
<td>Iib</td>
<td>C</td>
</tr>
<tr>
<td>Assessment of severity and prognosis</td>
<td>Iib</td>
<td>C</td>
</tr>
</tbody>
</table>


**Table 5. Recommendations for Cardiac Radionuclide Angiography**

<table>
<thead>
<tr>
<th>Indications</th>
<th>(1)</th>
<th>(2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assessment and follow-up of left ventricular function</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Monitoring of cardiac function in patients who are treated by cardiac toxicity agents</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Assessment of right ventricular function</td>
<td>Ila</td>
<td>B</td>
</tr>
<tr>
<td>Assessment of cardiac functions and shunts in patients with congenital heart disease</td>
<td>Iib</td>
<td>B</td>
</tr>
</tbody>
</table>

PET enables the quantitative evaluation of myocardial blood flow and the assessment of myocardial blood flow reserve. Thus, PET can be used for assessment of the severity of ischemic heart diseases and the quantitative diagnosis of myocardial microcirculatory disorders. PET can also be used for the detection of lesions in the early phase of arteriosclerosis and the determination of treatment effects.

Recommendations for F-18 FDG PET and myocardial perfusion PET are listed above (Table 6).

### 7. Stress Tests

Stress tests can be roughly divided into exercise stress tests and pharmacological stress tests. Dipyridamole, adenosine, and adenosine triphosphate (ATP) with a coronary dilation effect are used as pharmacological stress agents. Exercise stress tests are usually recommended and used if patients can exercise. Pharmacological stress tests are used in cases in which exercise stress tests are not suitable. It is important to understand the characteristics of stress tests and to evaluate the myocardial perfusion imaging taking into consideration symptoms during stress tests and ECG findings.

Recommendations for stress protocols are listed above (Table 7).

Beginning in June 2005, the government of Japan, through the National Health Insurance program, approved the use of adenosine as a stress agent for myocardial stress perfusion imaging and provided financial reimbursement for its use. Prior to this date the Ministry of Health, Labour and Welfare had not approved any agents for stress test myocardial perfusion imaging.

### 8. Characteristics and Precautions in Pediatric Cases

Indications of myocardial perfusion imaging in pediatric cases include congenital coronary artery diseases, acquired coronary artery diseases (mainly Kawasaki disease), cardiomyopathy, myocardial damage, and right ventricular pressure overload. Pharmacological stress tests may be more appropriate than exercise stress tests in many cases. It is necessary to consider the specificity of the imaging for pediatric cases when performing myocardial perfusion imaging and making a diagnosis in pediatric patients.

Recommendations for pediatric cases are listed above (Table 8).

### III Clinical Use of Radionuclide Imaging in Specific Cardiac Diseases and Pathologies

#### 1. Acute Coronary Syndrome

Tc-99m-labeled myocardial perfusion imaging is used for the diagnosis of chest pain suspected to be ACS. It has been reported that with the administration of Tc-99m-labeled myocardial perfusion agents in the acute phase, the imaging of an area of at-risk myocardium and the subsequent assessment of myocardial salvage by follow-up myocardial imaging are useful. However, there are a limited number of hospitals that provide Tc-99m-labeled myocardial perfusion imaging in the emergency department. Myocardial perfusion imaging performed in the early phase of ACS is important for risk stratification. It has been reported that diagnostic performance is improved by using myocardial perfusion imaging in combination with ECG gating.

The diagnostic accuracy of myocardial fatty acid metabolism imaging using I-123 BMIPP is equivalent to that of myocardial perfusion imaging in cases of acute myocardial infarction. I-123 BMIPP has higher diagnostic accuracy compared to rest myocardial perfusion imaging in cases of unstable angina. Myocardial imaging using I-123 BMIPP at rest is highly useful in patients with ACS in the early phase, which stress tests are difficult to perform (Table 9).

#### 2. Chronic Coronary Artery Diseases

Myocardial perfusion imaging is particularly useful for detecting coronary artery diseases in patients with intermediate pre-
Myocardial perfusion imaging and F-18 FDG PET are used in the assessment of myocardial viability. In order to determine myocardial viability in patients with reduced wall motion and a decreased LV ejection fraction, the presence or absence of a perfusion/metabolism mismatch is examined using myocardial perfusion imaging and F-18 FDG PET. In the case of a perfusion/metabolism mismatch with viable myocardium, adequate revascularization may improve wall motion, LV function and outcomes. F-18 FDG PET is useful in determining the indication of the revascularization procedure.

### References


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**Table 9. Recommendations for Cardiac Radionuclide Imaging in Acute Coronary Syndrome**

<table>
<thead>
<tr>
<th>Indications</th>
<th>Tests</th>
<th>Classification of recommendations</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis of myocardial infarction</td>
<td>TI-201, Tc-99m MPI</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Estimation of infarction size</td>
<td>TI-201, Tc-99m MPI</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Evaluation of revascularization effect</td>
<td>TI-201, Tc-99m MPI</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Diagnosis of unstable angina</td>
<td>I-123 BMIPP</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Differential diagnosis of chest pain</td>
<td>TI-201, Tc-99m MPI</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>Assessment of prognosis/risk stratification</td>
<td>TI-201, Tc-99m MPI</td>
<td>IIa</td>
<td>B</td>
</tr>
</tbody>
</table>

I-123 BMIPP, I-123-beta-methyl-p-iodophenylpentadecanoic acid; MPI, myocardial perfusion imaging.

**Table 10. Recommendations for Cardiac Radionuclide Imaging in Chronic Coronary Artery Diseases**

<table>
<thead>
<tr>
<th>Indications</th>
<th>Tests</th>
<th>Classification of recommendations</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detection of myocardial ischemia</td>
<td>Stress MPI</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Detection of viable myocardium</td>
<td>TI-201, Tc-99m MPI</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Assessment of cardiac function</td>
<td>Cardiac RNA, ECG gated SPECT</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Evaluation of revascularization effect</td>
<td>TI-201, Tc-99m MPI</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Risk assessment before non cardiac surgery</td>
<td>Stress MPI</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Assessment of prognosis/risk stratification</td>
<td>TI-201, Tc-99m MPI PET</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>Diagnosis of coronary vasospastic angina</td>
<td>I-123 BMIPP</td>
<td>IIa</td>
<td>C</td>
</tr>
</tbody>
</table>

ECG, electrocardiogram; I-123 BMIPP, I-123-beta-methyl-p-iodophenylpentadecanoic acid; MPI, myocardial perfusion imaging; PET, positron emission tomography; RNA, radionuclide angiography; SPECT, single-photon emission computed tomography.

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3. Heart Failure

While cardiac RNA has been widely used in the assessment of cardiac functions, the number of cardiac RNA studies has decreased with the improvement in accuracy of cardiac function measurement by echocardiography and the increased use of ECG gated SPECT. Quantitative gated SPECT (QGS) allows for the assessment of cardiac function during myocardial perfusion imaging.

Myocardial perfusion imaging can be used to determine the presence of ischemic versus nonischemic heart diseases as the cause of heart failure. It has been reported that the simultaneous assessment of myocardial blood perfusion and myocardial wall motion by ECG gated imaging improves diagnostic performance. Findings of myocardial perfusion abnormalities are also useful in the assessment of severity of heart failure. Myocardial sympathetic nerve imaging using I-123 MIBG is useful for assessment of severity, determination of treatment effects, and prediction of cardiac events.


Appendix

Chair:

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(To the affiliations of the members are as of September 2011)