

Normal values and standardization of parameters in nuclear cardiology: Japanese Society of Nuclear Medicine working group database

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Abstract As a 2-year project of the Japanese Society of Nuclear Medicine working group activity, normal myocardial imaging databases were accumulated and summarized. Stress-rest with gated and non-gated image sets were accumulated for myocardial perfusion imaging and could be used for perfusion defect scoring and normal left ventricular (LV) function analysis. For single-photon emission computed tomography (SPECT) with multi-focal collimator design, databases of supine and prone positions and computed tomography (CT)-based attenuation correction were created. The CT-based correction provided similar perfusion patterns between genders. In phase analysis of gated myocardial perfusion SPECT, a new approach for analyzing dyssynchrony, normal ranges of parameters for phase bandwidth, standard deviation and entropy were determined in four software programs. Although the results were not interchangeable, dependency on gender, ejection fraction and volumes were common characteristics of these parameters. Standardization of ¹²³I-MIBG sympathetic imaging was performed regarding heart-to-mediastinum ratio (HMR) using a calibration

phantom method. The HMRs from any collimator types could be converted to the value with medium-energy comparable collimators. Appropriate quantification based on common normal databases and standard technology could play a pivotal role for clinical practice and researches.

Keywords Japanese Society of Nuclear Medicine (JSNM) working group · Normal database · Myocardial perfusion imaging · ¹²³I-Metaiodobenzylguanidine (MIBG) quantification

Introduction

In nuclear cardiology, providing reliable results is a basis for clinical practice and research. Since nuclear cardiology has been based on functional imaging, a number of parameters have been calculated based on myocardial perfusion imaging (MPI), metabolism and sympathetic imaging [1]. While normal values are important from a physiological viewpoint, the values are influenced by methodologies used for measurements of specific cardiac parameters. Taking left ventricular (LV) ejection fraction (EF) as an example, differences in the quantitative value exist among echocardiography, left ventriculography with contrast media, magnetic resonance imaging and X-ray computed tomography (CT), and some differences have been noticed even with nuclear imaging, including gated blood-pool study and gated MPI using single-photon emission computed tomography (SPECT) [2, 3]. The results also vary depending on the software used for analysis, in which Quantitative Gated SPECT/Quantitative Perfusion SPECT (QGS/QPS, Cedars Sinai Medical Center, Los Angeles, CA, USA), Emory Cardiac Toolbox

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(ECTb, Emory University/Syntermed Inc., Atlanta, GA, USA), and 4DM-SPECT/Corridor 4DM (Michigan University/INVIA, LLC, Ann Arbor, MI) are included [4–7]. In Japan, two software programs of Heart Function View/Heart Score View (HFV/HSV, Nihon Medi-Physics Co. Ltd., Tokyo, Japan) [8, 9] and cardioREPO (FUJIFILM RI Pharma, Co. Ltd., Tokyo, Japan/EXINI Diagnostics, Lund, Sweden) have also been developed [10]. When we overview a variety of software programs, the threshold of LVEF is critical not only for differentiation of normal versus abnormal LV function, but also for prognostic purposes [11–13], since a large number of patients could be included in the borderline range from 50 to 60%.

JSNM working group activities in 2007 and 2015

Both normal values and tracer distributions are important in myocardial SPECT imaging. Patient-related factors, such as sex and body habitus, may influence tracer distribution. In addition, various technical factors may also be of concern such as SPECT equipment, rotation range of camera heads, collimator types, scatter and attenuation corrections and crystal types, namely sodium iodide (NaI) or cadmium zinc telluride (CZT) [2].

The Japanese Society of Nuclear Medicine (JSNM) working group created SPECT databases for myocardial perfusion imaging, fatty acid and sympathetic imaging, and have provided normal files fitted for various software programs (JSNM working group database 2007) [14–16]. The normal MPI studies were defined as subjects with low likelihood of cardiac diseases with no evidences of the

following conditions: underlying known cardiac diseases, electrocardiographic (ECG) evidence of ischemia or infarction, wall motion abnormality, arrhythmia inappropriate for gating and those with medications for hypertension and diabetes. Both patients who had normal coronary angiography and those who were not indicated for coronary angiography because of a low possibility of coronary artery disease were included. The MPI studies were performed with a standard dose of ^{99m}Tc -methoxyisobutylisonitrite (MIBI)/tetrofosmin (555-1110MBq) and ^{201}Tl (74-111MBq).

In the working group database 2007, the databases were separately created for rotation range ($180/360^\circ$), gender, stress and rest, and radiopharmaceutical types including ^{99m}Tc -MIBI/tetrofosmin, ^{201}Tl , ^{123}I -beta-methyliodophenylpentadecanoic acid (BMIPP) and ^{123}I -meta-iodobenzylguanidine (MIBG) (Table 1). The collimator difference was only taken into considerations for planar ^{123}I -MIBG imaging. As a result of the working group activity, normal databases applicable to conventional non-attenuation corrected SPECT could be used in any hospitals in Japan, and the initial multicenter validation showed comparable diagnostic accuracy to expert reading of MPI [17].

Subsequent working group activity of “Creation of common databases in nuclear cardiology and cross-calibration among software programs” began in October 2013, and a 2-year project was conducted (Table 2). In the current working group activity, data sets of gated and non-gated MPI were collected, and new SPECT databases of ^{201}Tl and ^{99m}Tc -MIBI or tetrofosmin with multifocal

Table 1 Achievements of JSNM working group activities in 2007 and 2015

Normal database types	JSNM working group 2007	JSNM working group 2015
Normal perfusion database at stress and rest	-SPECT databases specific for gender, ^{99m}Tc MIBI/tetrofosmin and ^{201}Tl , and camera rotation ranges ($180/360^\circ$) -Only with exercise stress	-Adenosine stress included -Increased number of databases with a complete set of gated and non-gated data
Databases for multifocal collimators with IQ-SPECT	-Not done	-Databases for supine, prone, and CT-based attenuation correction
Databases for fatty acid imaging	- ^{123}I -BMIPP SPECT databases specific for gender and rotation ranges ($180/360^\circ$)	-Not done
Databases for sympathetic imaging	- ^{123}I -MIBG SPECT databases specific for gender, rotation ranges ($180/360^\circ$), and early and late imaging -Planar anterior images specific for LE and ME/LME collimators	-Cross-calibration of ^{123}I -MIBG HMR with all possible collimator types based on calibration phantom experiments -MIBG defect scoring for new software programs
Validations with software programs	-Normal ranges of LVEF, volume and diastolic parameters -Comparison between Japanese and US databases	-Normal ranges of LVEF, volume and diastolic parameters (recalculated) -Normal values of phase dyssynchrony parameters in four software programs

SPECT single-photon emission computed tomography, HMR heart-to-mediastinum ratio, LVEF left ventricular ejection fraction, LE low energy, ME medium energy, LME low medium energy, US United States

Table 2 Working group and collaborated researchers

Working group members	
Kenichi Nakajima	Kanazawa University, Chief of the working group
Naoya Matsumoto	Nihon University Hospital
Tokuo Kasai	Tokyo Medical University Hachioji Medical Center
Keisuke Kiso	National Cerebral and Cardiovascular Center
Mitsuru Momose	Tokyo Woman's Medical University
Masayasu Nakagawa	Akita City Hospital
Masao Miyagawa	Ehime University
Kenji Uchida	Tokyo Medical University
Shinro Matsuo	Kanazawa University Hospital
Masahisa Onoguchi	Kanazawa University School of Health Science
Koichi Okuda	Kanazawa Medical University
Collaboration for data collections	
Chisato Kondo	Tokyo Woman's Medical University
Masayoshi Sarai	Fujita Health University Hospital
Yoriko Horiguchi	Sagamihara National Hospital
Collaboration regarding data processing and software preparation	
Ernest Garcia	Emory University, Atlanta, GA, USA; Syntermed Inc. Atlanta, GA, USA
Shimizu Takeshi	Siemens Japan, Tokyo, Japan
Kazunori Kobayashi	Nihon Medi-physics, Co. Ltd., Tokyo, Japan
Takehiro Ishikawa	Fujifilm RI Pharma, Tokyo, Co. Ltd, Japan
Lars Edenbrandt	University of Gothenburg, Gothenburg; EXINI Diagnostics, Lund, Sweden
Edward Ficaro	University of Michigan Health System; INVIA Medical Imaging Solutions, LLC, Ann Arbor, MI, USA

collimation (IQ-SPECT, Siemens, Japan/USA) were added. In the additional databases, both exercise and pharmacological stresses were included, and well-controlled patients with single medication for hypertension, dyslipidemia and diabetes mellitus could be included. Normal values were determined for each software program and applied to clinical practice and works of research. Recently, although new software of phase analysis has been developed [18], normal values of the phase parameters have not been presented in Japan. We therefore decided on all normal phase dyssynchrony parameters including HFV and cardioREPO software, which are commonly used in Japan. A project of standardization of ^{123}I -MIBG heart-to-mediastinum ratio (HMR) was also performed using the calibration phantom method [19, 20] as well as defect scoring based on a 17-segment polar map display [21, 22].

Normal myocardial perfusion databases in the JSNM working group 2015

The characteristics of normal MPI databases are summarized in Table 3 in the Japanese population including ^{201}Tl and $^{99\text{m}}\text{Tc}$ -perfusion tracers. Inclusion of ^{201}Tl databases

reflected the recent situations in Japanese nuclear medicine practice. Recently in North America and Europe, $^{99\text{m}}\text{Tc}$ -MIBI and tetrofosmin have been widely used, and the use of ^{201}Tl has been limited [23]. This has contributed to reduced radiation exposure due to nuclear imaging, and dual-isotope imaging has been discouraged. On the other hand, in Japan, half of the MPI study has been performed with ^{201}Tl as of 2015. The background of this trend in Japan is due to composite factors in favor of ^{201}Tl , which include better tracer extraction fraction, better defect contrast, sufficient image quality even with a dose of 74–111 MBq, and single administration for both stress and rest studies. However, $^{99\text{m}}\text{Tc}$ radiopharmaceuticals are more appropriate for 16-frame gating, rather than 8-frame gating, and have better physical characteristics for imaging. Moreover, from the viewpoint of radiation exposure and the possibility of stress-only study, when the study is very normal [24, 25], the use of $^{99\text{m}}\text{Tc}$ tracers will be increased in Japan.

As another characteristics of Japanese database, both 360° and 180° rotation acquisition databases were separately created. Although the 360° acquisition is still widely used in Japan with multi-detector systems, most of the

Table 3 Characteristics of MPI databases

	<i>N</i> , mean ± SD, range
Number of data	285
Number of hospital	9
^{99m} Tc or ²⁰¹ Tl (<i>N</i>)	^{99m} Tc 206, ²⁰¹ Tl 79
^{99m} Tc-MIBI or tetrofosmin (<i>N</i>)	MIBI 110, Tetrofosmin 95
180° or 360° (<i>N</i>)	180° 169, 360° 116
Number of RR division (<i>N</i>)	16 frames 206, 8 frames 79
Sex (<i>N</i>)	Male 145, Female 140
Age (years)	65 ± 12 (range 16–88)
Male	
Height (cm)	166 ± 6
Weight (kg)	63 ± 10
Body mass index (kg/m ²)	22.7 ± 3.3 (range 15.7–33.7)
Female	
Height (cm)	154 ± 6
Weight (kg)	53 ± 8
Body mass index (kg/m ²)	22.1 ± 3.1 (range 16.2–35.6)
Exercise or pharmacological stress	Exercise 182, Adenosine 30, Exercise + Adenosine 73
Exercise: heart rate (/min)	131 ± 21
Exercise: systolic blood pressure (mmHg)	193 ± 32
Exercise: diastolic blood pressure (mmHg)	93 ± 22

Number of IQ-SPECT databases is not included

cardiac studies are performed with a 180° acquisition in North America and Europe. When Japanese MPI studies with a 360° rotation acquisition were analyzed regarding perfusion defect scores with QGS, the 360° rotation acquisition database provided higher diagnostic accuracy compared with databases from a 180° rotation acquisition in the Japanese and American populations [26].

The normal perfusion databases are essential for appropriate quantification of perfusion defects. Since defect scores as summed stress/rest/difference scores (SSS/SRS/SDS) depend on normal databases and software algorithms, agreement among various software types is considered desirable, but non-negligible difference in scores does exist. Figure 1 shows a patient who showed a mild to moderate degree of ischemia, when QGS, HSV and cardioREPO are used for quantification. The scoring of SSS ranged from 6 to 9, showing only minor differences. Since the threshold of 10 % ischemia has been recognized as the indication for coronary intervention when coronary stenosis is >50 % [27–29], similar quantitative results at least regarding this threshold are desirable, and further comparative studies are required.

Myocardial perfusion database for short-time acquisition protocols

There are two possibilities for short-time acquisition protocols, namely multifocal collimation with IQ-SPECT

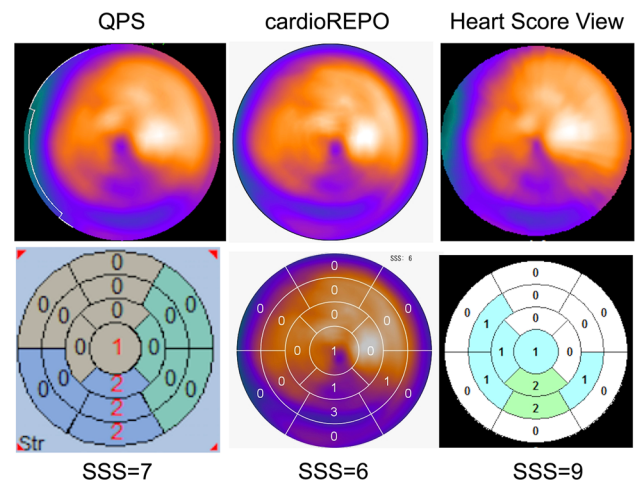


Fig. 1 Polar perfusion maps and summed stress score (SSS) calculated by QGS, cardioREPO and Heart Score View (HSV). The patient had significant stenosis (90 %) in the right coronary artery, and an inferior low perfusion area is shown in the stress image

(SMARTZOOM collimator; Siemens, Tokyo, Japan) and CZT camera of either D-SPECT (Biosensors Japan/Dynamic Spectrum, Israel; installed in 8 institutions as of December 2015) or NM530c (GE healthcare, Japan; installed in 8 institutions). This working group created databases for IQ-SPECT, and the database for CZT camera was investigated in another JSNM working group in 2014. Compared with the Anger camera, the CZT camera

demonstrated dramatically higher performance, and the IQ-SPECT system with special cardiac-dedicated collimation also increased heart counts by focal magnification [30]. The CZT camera provided comparable diagnostic accuracy as assessed by fractional flow reserve [31]. Combined use of supine and prone imaging for detecting coronary artery disease using the scoring method was effective for accurate diagnosis [32], and additional automatic quantification based on standard databases is expected.

The IQ-SPECT system used multifocal collimators and achieved 4 times higher counts in the heart compared with the conventional parallel-hole collimator system [30, 33–35]. With the collaboration of IQ-SPECT users, ^{201}Tl normal databases in supine and prone positions and CT-based attenuation correction were created with scatter correction and ordered subset conjugate gradient minimization reconstruction [36]. Additional $^{99\text{m}}\text{Tc}$ -MIBI/tetrofosmin databases will be completed in 2016. IQ-SPECT images show slightly different distribution of the radiotracer due to its specific collimation (Fig. 2). The prone position showed a higher count in the inferior walls than the supine position, and gender difference was observed. In contrast, CT-based attenuation correction demonstrated more homogeneous distribution of each wall, while the apical segment showed significantly decreased activity in both genders. These observations are common characteristics seen in attenuation-corrected SPECT images with parallel-hole collimation [37, 38]. The decreased apical wall activity is partly due to the physiologically thin apical wall and larger apical wall movement [39]. Although attenuation correction was considered potentially useful and recommended [40], its use is still limited in Japan, because nuclear medicine physicians and cardiologists have become accustomed to using conventional imaging without attenuation correction and inconsistency of the effects of attenuation correction regarding camera systems and processing tools [41]. However, since stress-only imaging in combination with attenuation correction is effective to appropriately identify low-risk patients [24, 25], and true quantification in a unit of Bq/ml is a goal of radioactivity measurement in SPECT, a CT-based attenuation correction approach should be further pursued.

Normal values of LV function based on the updated gated SPECT databases

Normal values of LVEF and volumes were the basis for evaluating cardiac function in various cardiac diseases [2, 16]. According to the JSNM working group databases (2007), EF was calculated higher for females than males with QGS, and lower limits were approximately 50 % for males and 55 % for female patients, which were slightly higher compared with the study in the United States and

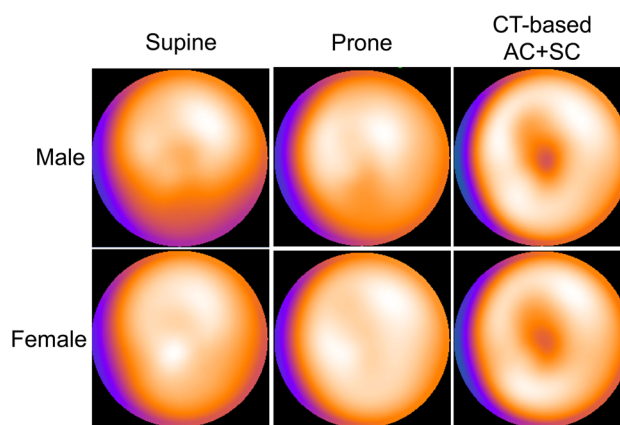


Fig. 2 IQ-SPECT normal databases created with supine and prone positions, and CT-based attenuation correction (AC) and scatter correction (SC). After CT-based correction, gender difference was not observed

Europe [14]. The normal values at rest created by the current JSNM database (2015) are shown using QGS software in Tables 4 and 5. In small hearts, however, underestimation of the true volume occurs and the effect is higher for ESV than for EDV, resulting in an increase in LVEF. This small-heart artifact is caused by the SPECT reconstruction method optimized for blurred myocardial walls. To minimize such artifacts, particularly in female subjects and children, cardioREPO has adopted a corrected algorithm for small hearts [16]. Average and standard deviation (SD) calculated in 69 subjects are shown in Fig. 3, focusing on the difference in software types.

Normal ranges of phase dyssynchrony parameters

Since four software programs are now available in Japan, normal values of the phase parameters were compared. Phase analysis has been used for more than 30 years using a planar gated blood-pool study. Fourier transform was applied to time-activity curves of each pixel, and phase and amplitude of the fundamental frequency were displayed as functional maps. The method was also used for gated blood-pool SPECT, and three-dimensional propagation patterns of phase were analyzed in patients with conduction anomalies and ventricular asynergy [42, 43]. Subsequently, the method was also applied to gated MPI, in which a proportionate relationship between count and wall thickness due to a partial volume effect was used for myocardial time-activity curves [44, 45]. Indications for cardiac resynchronization therapy (CRT) might be one of the promising applications [46, 47]. Although a number of parameters were proposed, most of the echocardiographic parameters lack validation in appropriate clinical settings, indicating striking variability, poor reproducibility, and limited predictive power [48, 49]. Whether a nuclear

Table 4 Normal values for LV volume, EF and diastolic parameters at rest using ^{99m}Tc MIBI/tetrofosmin MPI (16-frame gated study)

	Male	SD	Lower limit	Upper limit	Female	SD	Lower limit	Upper limit	<i>P</i>
<i>N</i>	106				100				
EF (%)	66.9	6.6	54	80	75.1	7.6	60	90	<0.0001
EDV (mL)	80.8	19.6	42	120	59.0	13.6	32	86	<0.0001
ESV (mL)	27.3	9.9	8	47	15.2	7.2	1	30	<0.0001
EDVI (mL/m ²)	47.8	10.1	28	68	39.4	7.5	24	54	<0.0001
ESVI (mL/m ²)	16.2	5.5	5	27	10.0	4.3	1	19	<0.0001
Diastolic									
PFR (/s)	2.42	0.52	1.38	3.45	2.87	0.63	1.61	4.12	<0.0001
1/3MFR (/s)	1.39	0.32	0.74	2.03	1.59	0.34	0.91	2.27	<0.0001
TPFR (ms)	175	33	108	241	165	30	106	224	0.024
TPFR/RR	0.19	0.05	0.09	0.29	0.18	0.03	0.12	0.25	0.42
Diastolic (age ≤65y)									
<i>N</i>	52				42				
PFR (/s)	2.57	0.49	1.58	3.55	2.96	0.67	1.63	4.30	0.0011
1/3MFR (/s)	1.49	0.32	0.85	2.13	1.65	0.33	0.99	2.32	0.014
TPFR (ms)	169	27	115	223	161	28	105	217	0.15
TPFR/RR	0.19	0.05	0.09	0.29	0.18	0.03	0.12	0.25	0.36

Lower and upper limits were calculated by mean \pm 2SD

All values are based on QGS software

EF ejection fraction, EDV end-diastolic volume, ESV end-systolic volume, EDVI EDV index, ESVI ESV index, PFR peak filling rate, MFR, 1/3MFR one-third mean filling rate, TPFR time to PFR, TPFR/RR, TPFR divided by RR interval

Table 5 Normal values for LV volume and EF at rest using ^{201}Tl MPI (8-frame gated study)

	Male	SD	Lower limit	Upper limit	Female	SD	Lower limit	Upper limit	<i>P</i>
<i>N</i>	39				40				
EF (%)	61.9	6.3	49	74	66.4	8.1	50	83	0.0067
EDV (mL)	69.8	14.2	41	98	60.8	11.0	39	83	0.0023
ESV (mL)	26.9	7.9	11	43	20.8	7.4	6	36	0.0007
EDVI (mL/m ²)	41.6	8.2	25	58	40.6	7.5	26	56	0.56
ESVI (mL/m ²)	15.9	4.6	7	25	13.9	5.0	4	24	0.066

Abbreviations are the same as in Table 3.

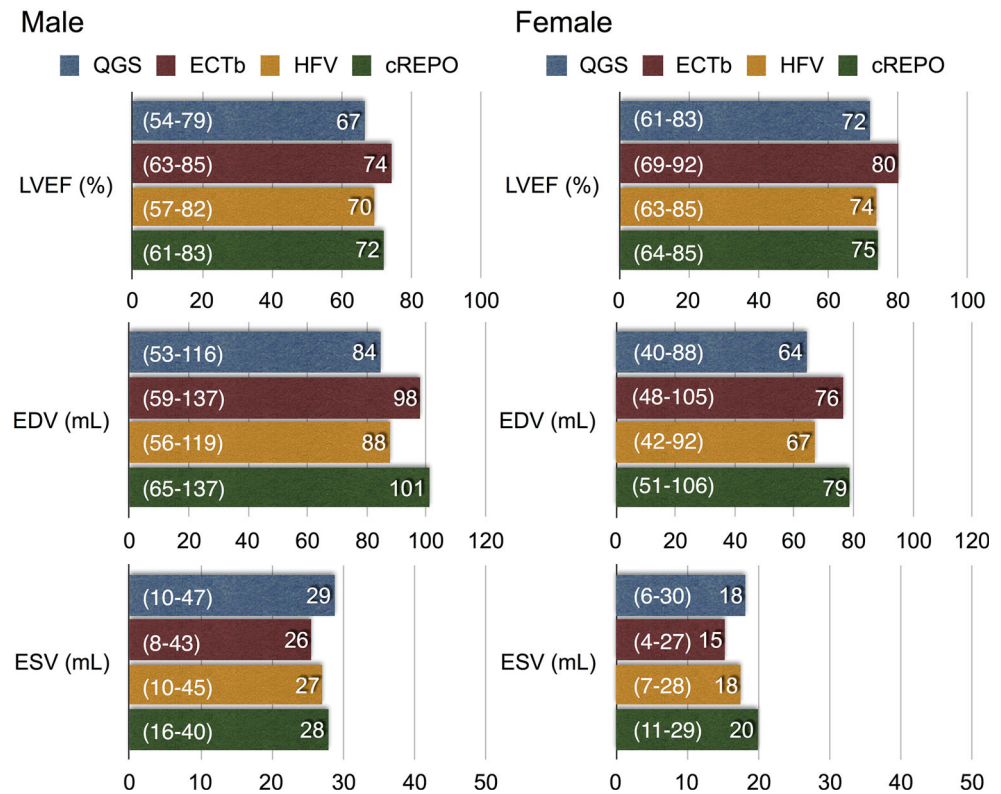
All values are based on QGS software

approach provides robust results over ECG and LVEF should be further investigated in patients who are indicated for CRT.

When the same original data are provided, nuclear medicine approach generally shows good reproducibility or precision for LVEF and volumes and good correlation to values derived from other modalities. In phase parameters, however, normal values were still not validated well. The working group activity therefore included determination of normal values of phase parameters for ECTb, QGS, HFV and cardioREPO (Fig. 4) [50]. Based on distribution of phase values in the LV, phase histogram is created, and parameters of phase bandwidth, in which 95 % of the phase distribution is included, phase standard deviation (PSD) and phase entropy are calculated. Phase entropy is an index of “disorder” defined by

summation of $[f_i \cdot \log(f_i)] / \text{Log}(n)$, where f and n are frequency in the i -th bin and number of bins, respectively, which ranges from 0 to 1 (0–100%). When the normal values were determined at rest based on the working group database, the results could not be interchangeably used. However, some similarities in normal ranges existed between ECTb and cardioREPO and between QGS and HFV, which probably depended on the computation algorithm of each software program. The upper limit of PSD was 20° for ECTb and cardioREPO, and 10° for QGS and HFV. All software programs showed higher PSD and bandwidth in male subjects than in female subjects. In addition, the higher SD and bandwidth were related to the larger LV volume and the lower EF, which depended on software types. Finally, since the upper limit of the normal values was not the best threshold for the

Fig. 3 Gated SPECT parameters of EF, EDV and ESV at rest calculated with four software programs, namely QGS, ECTb, cardioREPO (cREPO) and HFV, in the JSNM normal databases. Mean values and range (mean \pm 2SD in brackets) are written in bars. The figure is adapted from Table 1 in Ref. [50]



effective indication to CRT [47], the optimal threshold should be separately validated.

Standardization of ^{123}I -MIBG HMR for multicenter studies

^{123}I -MIBG has a long history of clinical use in Japan since 1992, and major indications have been chronic heart failure (CHF) and Lewy-body diseases [51]. Regarding application of MIBG in CHF, a number of studies in Japan, Europe and the United States have unanimously shown that low HMR and high washout rate (WR) were related to poor outcomes including cardiac death, progression of heart failure and occurrence of lethal arrhythmia [51–55]. In multicenter studies and meta-analysis, the threshold of HMR for poor prognosis was around 1.6–1.8. In contrast, patients who showed HMR >2.0 showed good prognosis. However, it has been understood that significant differences in HMR exist among hospitals depending on scintiscanners and collimators [20, 56, 57]. In the JSNM working group normal databases, while average late HMR with a low-energy (LE) collimator was 2.5, that with a medium-energy (ME) collimator was 3.0 [1]. To obtain stable results, the recommendation of European Association of Nuclear Medicine Cardiovascular Committee and European Council of Nuclear Cardiology was to use the ME-type collimator [58]. However, in clinical practice a number of hospitals continue to use the LE high-resolution

(HR) collimator in Europe and North America, and LE general purpose (GP) or low-medium energy (LME) has also been widely used in Japan.

To adjust the differences in camera-collimators, while the multi-energy window acquisition method and direct empirical correction method have been proposed, they were not practical for applying the method to all possible camera-collimator conditions. The calibration phantom method was developed in Japan, which used specific phantoms to obtain two HMRs from anterior and posterior views [59]. Based on the phantom experiments in each institution, the conversion coefficient in each camera-collimator system was determined, and all the HMRs could be converted to the condition of the most common ME general purpose (GP) collimator with a conversion coefficient of 0.88 [19] (Table 6). The linear regression equation among the system used the formula passing on the coordinate of HMR (1,1). It is based on the assumption that HMR should be 1, when cardiac activity is equal to mediastinal activity. The experiments have already been performed in 500 hospitals in Japan, and in more than 30 camera-collimator conditions in Europe as of the end of 2015.

When the threshold HMR was converted to the condition of the MEGP collimator, the threshold of ADMIRE-HF (1.6, with LEHR), Sapporo Medical University (1.74, with LEGP) and the pooled database in Japan (1.68, with LE collimators in 6 hospitals) were converted to around 2.0 [51]. In a neurology field, the thresholds of differentiating

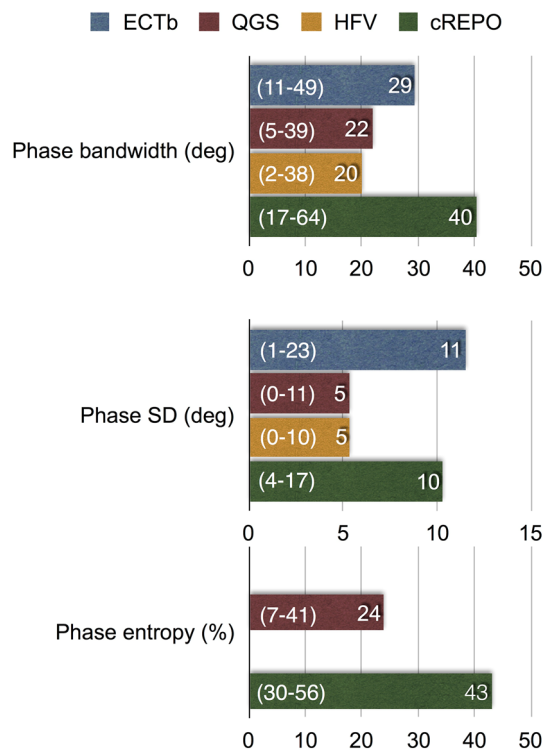


Fig. 4 Comparison of phase parameters (phase bandwidth, phase SD, and phase entropy) at rest with four software programs using the JSNM normal databases. Mean values and range (mean \pm 2SD in brackets) are written in bars. The figure is adapted from Table 2 in Ref. [50]

Alzheimer disease and dementia with Lewy bodies were 2.0–2.2 in a multicenter study in Japan [60]. The effectiveness of standardization included not only diagnosis but also prognostic evaluation. The mortality rate in the Japanese pooled database was analyzed, and 2 and 5-year mortality risk models were created [61, 62]. In this multivariate model, parameters of age, sex, LVEF, New York Heart Association functional class, and late HMR were used. In addition, since ^{123}I -MIBG WR differs significantly based on the use of background and decay correction and timing of late imaging, standardization of methodology is also required for calculating WR [63].

With the advent of the CZT camera, ^{123}I -MIBG planar image may not be a part of clinical routine study. D-SPECT, however, provides a planogram comparable to

the planar anterior view [64]. Based on these reconstructed planar images, HMR can be similarly calculated, although the camera field of view is narrow. When HMRs from the D-SPECT and the Anger camera were compared, a linear relationship was obtained. Moreover, when the Anger image HMR was standardized to HMR with the ME condition as proposed, both D-SPECT and planar standardized methods showed similar HMR values, indicating feasibility of standardization in including planar and SPECT studies [64, 65].

^{123}I -MIBG defect scoring using normal SPECT databases

The degree of segmental defect in ^{123}I -MIBG SPECT can be scored using a similar 17-segment model used for MPI. Although visual scoring can be used, the distribution of ^{123}I -MIBG differs significantly in myocardial walls, showing lower count particularly in the inferior region. Although comparative scores between perfusion and ^{123}I -MIBG have been used [22], appropriate databases are particularly important for ^{123}I -MIBG imaging. The JSNM working group created ^{123}I -MIBG databases for the first time to quantify defect scores and is clinically available now [1, 15] (Fig. 5). Moderate agreement could be observed between HMR and defect scores. However, the problem of defect scoring was in patients with a general decrease in the whole heart, since the scoring implicitly assumes that normal myocardial remains in some segments of the myocardium [66]. A new idea for scoring is necessary when HMR is very low in a whole heart, which is sometimes seen in Lewy-body diseases and severe heart failure. At present, defect scoring has a complimentary role for evaluating the severity of three-dimensional ^{123}I -MIBG defects.

Importance of normal database and future trends

Standardized viewpoints based on normal databases are important for appropriate diagnosis in heart diseases. The JSNM working group provided information on normal control values and database sets as well on clinical works and research. Recently, conventional SPECT systems have been upgraded to SPECT-CT, which created different

Table 6 Normal HMR after standardization to ME-collimator condition (conversion coefficient = 0.88)

	Average	Range
Early HMR	3.1	2.2–4.0
Late HMR	3.3	2.2–4.4
Washout rate (decay and background corrected)	13	0–34 %

Average conversion coefficients were 0.55 for LEHR collimator, 0.65 for LEGP collimator, 0.65 or 0.75 for extended LEGP collimator (depending on types), 0.83 for LMEGP collimator, 0.88 for MEGP collimator and 0.95 for ME low penetration collimator [19]

HMR heart-to-mediastinum ratio, WR washout rate

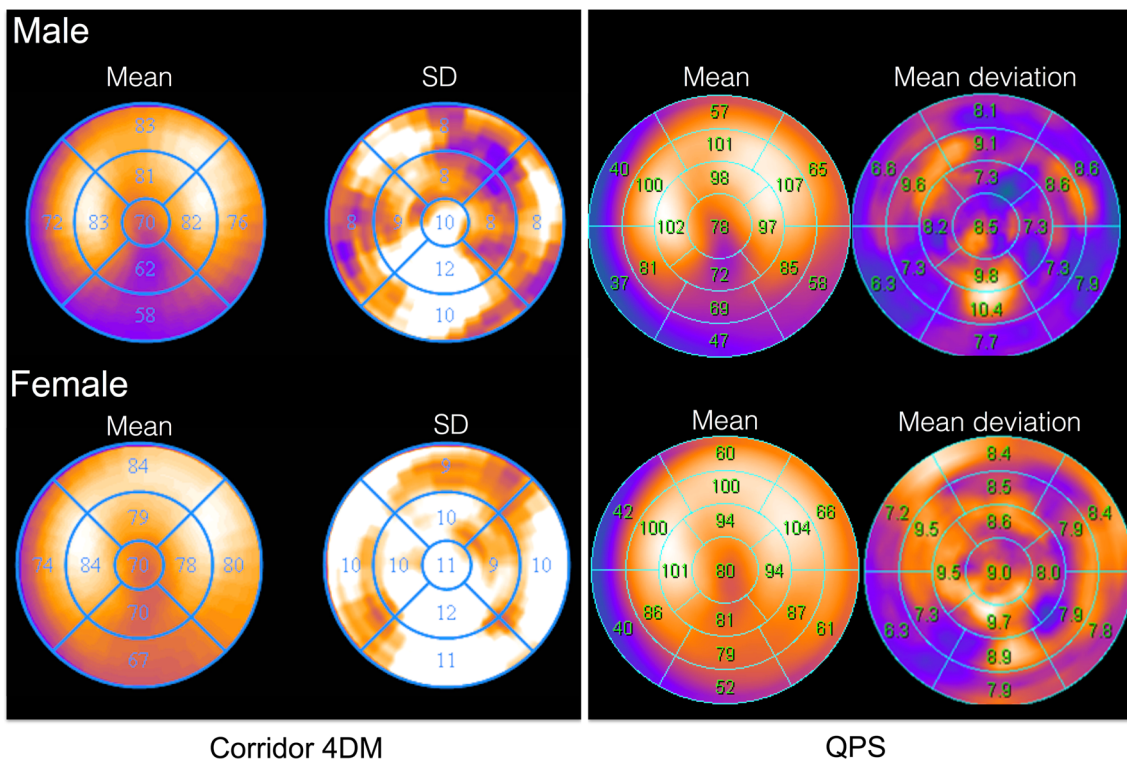


Fig. 5 Average distribution of late ^{123}I -MIBG image on polar maps with Corridor 4DM and QPS software. Similar distributions in the mean and deviations are noted between two software programs. *SD* standard deviation

distribution patterns by CT-based attenuation corrections. In addition, solid-state cameras provide specific count distributions in the myocardium in addition to high resolution and sensitivity. Although we could not create all possible normal databases in this working group activity, common standard databases created by JSNM will contribute to standard interpretation of nuclear images. Moreover, since amount of ischemia is used for diagnostic threshold for the indications of coronary intervention, it is convenient if at least the diagnostic threshold determined by different software shows similar defect scores.

Phase parameters were determined in JSNM working group activity. However, it should be further investigated whether a nuclear approach shows advantages over conventional criteria using ECG and LVEF or echocardiography.

Regarding standardization of ^{123}I -MIBG HMR, conversion to MEGP-collimator comparable values is occurring in Japanese hospitals. Various collimators including LEHR, LEGP, extended LE, MEGP and ME low penetration collimators are used at present in Japan. Although the HMR is a simple parameter of planar count ratio of the heart to background regions, it is important to consider that a minor difference potentially creates significant differences in prognosis. If correlation to SPECT methods and planar HMR becomes clear, wider application of MIBG

can be anticipated using the standardized parameters. Since we found good correlation between D-SEPCT and standardized HMR using the Anger camera, creation of large standardized databases would be feasible after standardization. In future studies, clinical use of ^{123}I -MIBG imaging should incorporate individual patient risk stratification and determine roles for therapeutic decision-making in patients with CHF [51, 67].

Conclusion

The JSNM working group of nuclear cardiology created common normal databases fitted for conventional SPECT system and SPECT-CT imaging with multifocal collimators. While quantification by nuclear medicine software is supported by the normal values, the values are not interchangeable for any software types and the characteristics of the calculated parameters should be kept in mind for clinical application.

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Compliance with ethical standards

Conflict of interest KN has collaborative research with Fujifilm RI Pharma Co., Ltd., which supplies ^{123}I -MIBG in Japan and developed software. KN also was involved in developing cardiac software with Nihon Medi-Physics (Tokyo, Japan).

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