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Comparisons and Contrasts in the Practice of Nuclear Cardiology in the United States and Japan

E. Gordon DePuey, MD

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Abstract

There are interesting differences between the practice of Nuclear Cardiology in Japan and that in the United States and associated unique challenges. Differences in patient body habitus and the perceived importance of limiting patient radiation dose have resulted in different radiopharmaceutical and imaging protocol preferences. Governmental approval and reimbursement policies for various radiopharmaceuticals have promulgated adoption of different clinical applications. Both countries have experienced a significant decline in the number of nuclear cardiology studies performed, in part due to decreased governmental funding and reimbursement and to the emergence of competing modalities. Whereas precertification and test substitution have impacted negatively on the sustainability and growth of nuclear cardiology in the United States, in Japan those deterrents have not yet been encountered. Instead, communication barriers between nuclear medicine physicians and referring cardiologists are cited as being of greater significance.

Keywords: Clinical practice, Japan, Nuclear cardiology, United States
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Last year in the *Journal of Nuclear Cardiology*, Yoshinaga et al. published an excellent report of the current status of nuclear cardiology in Japan (1). In November, I had the opportunity to speak at the annual scientific meeting of the Japanese Society of Nuclear Medicine (JSNM) in Tokyo and to update our colleagues there on the status of nuclear cardiology in the United States. Shared thoughts and opinions regarding the similarities and contrasts in practices in the two countries were enlightening.

The population of the United States is approximately 320 million, compared to 125 million in Japan. Coronary artery disease diagnosis, prevention, and treatment constitute major health care initiatives in both countries. Both Japanese and American investigators have been actively involved in research since the inception of our field and have contributed considerably to the peer-reviewed literature. Citizens of both countries have access to state-of-the-art nuclear cardiology. Just as the American Society of Nuclear Cardiology (ASNC), the Society of Nuclear Medicine and Molecular Imaging (SNMMI), and the American College of Cardiology (ACC) have set forth guidelines for the clinical use of nuclear cardiology procedures, the Japanese Circulation Society (JCS) in 2010 established Guidelines for the Clinical Use of Cardiac Nuclear Medicine, including myocardial perfusion single-photon emission computed tomography (SPECT) (2). Indications common to both countries include the diagnosis of myocardial ischemia and infarction, assessment of the severity of coronary artery disease, assessment of myocardial viability, determination of the indication for coronary revascularization, and assessment of treatment effects. Nevertheless, due to patient population characteristics, the health care reimbursement environment, and approval of new radiopharmaceuticals, there are substantial differences in the practice of nuclear cardiology in the two countries.

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E. Gordon DePuey
Division of Nuclear Medicine, Department of Radiology, Mt. Sinai St. Luke's and Mt. Sinai West Hospitals, Icahn School of Medicine at Mt. Sinai, New York, NY, USA
E-mail: EDepuey@CHPNET.ORG

Differences in nuclear cardiology practice in Japan and the United States

Some of the very basic aspects of the practice of nuclear cardiology differ considerably in Japan and the United States (US). In the US 86% of myocardial perfusion SPECT scans are performed with either technetium-99m (^{99m}Tc) sestamibi or tetrofosmin. Thallium-201 (^{201}Tl) is used for the remaining 14%. Rest-delayed thallium and dual isotope protocols have been strongly discouraged due to high patient radiation dose, well above the ASNC guideline of less than 9 mSv in 50% of the population (3, 4). In addition, photon attenuation and scatter in patients with large chests generally render ^{201}Tl SPECT suboptimal. In contrast, in Japan, where obesity is uncommon and patients are generally smaller, ^{201}Tl provides good SPECT image quality. Japanese nuclear physicians are indeed attentive to patient radiation dose reduction (5, 6); however, implementation of reduced-dose strategies has not been as proactively pursued as it has been in the US and Europe.

Interestingly, other differences between the practices of nuclear cardiology in Japan and the US are more a consequence of governmental approvals and certifications than of the needs of the respective populations. In Japan, in addition to radiopharmaceuticals for myocardial perfusion imaging, the Japanese Ministry of Health, Labor and Welfare (JMHLW) approved iodine-123-metaiodobenzylguanidine (^{123}I-MIBG) in 1992 as a myocardial enervation agent. This application supplements its widespread use in the aging Japanese population to differentiate Alzheimer's dementia from Lewy body dementia. Also iodine-123-beta-methyl-p-iodophenylpentadecanoic acid (^{123}I-BMIPP) was approved in 1996 as an ischemic memory agent. There is extensive Japanese literature investigating and documenting the applicability of these agents, and they are currently in widespread clinical use (7). In contrast, in the United States ^{123}I-MIBG was approved by the Federal Drug Administration just a few years ago (8). However, its cost is very high and reimbursement is comparatively low; therefore, the radiopharmaceutical is seldom used clinically. ^{123}I-BMIPP is not approved for clinical use in the United States. In Japan N-13 ammonia (^{13}N-NH_3) was just approved in 2012 for PET myocardial perfusion imaging, but can be used only when SPECT myocardial perfusion imaging is equivocal or non-diagnostic. O-15-labeled water (^{15}O-H_2O) has been approved for radionuclide angiocardiography, and F-18 fluorodeoxyglucose (^{18}F-FDG) has been approved for the evaluation of myocardial viability (9). In contrast, in the US, the radiopharmaceutical rubidium-82 (^{82}Rb) is by far the most commonly used for myocardial perfusion PET. However, in Japan it is not yet approved by the JMHLW and has been applied, for research purposes only, to a limited number of patients with coronary artery disease (CAD). ^{18}F-FDG has been used extensively in Japan for the diagnosis of cardiac sarcoid, and its use is now gradually increasing in the United States.

In Japan, reimbursement is determined according to the particular disease and the clinical circumstances (emergent, elective, etc.). This system is called the Diagnostic Procedure Combination (DPC), similar to the Diagnostic Related Group (DRG) system in the United States. However, it differs significantly from the United States system, in which the appropriateness and consequent reimbursement of each procedure are highly scrutinized by third party payers.

In both the United States and Japan, the use of myocardial perfusion SPECT is closely tied to the use of percutaneous coronary intervention (PCI). However, in contrast to the practice in the United States, in Japan the use of elective PCI is greater than that of emergent PCI. For example, in 2014 according to the US National Cardiovascular Data Registry (NCDR) CathPCI Registry, non-acute PCI was performed in 59,375 cases (14%), whereas emergent PCI was performed in 374,543 cases (86%) (10). In contrast, in the same year, the Japanese Registry of All Cardiac and Vascular Diseases (JROAD) reported 185,116 non-acute PCIs (73%) and only 68,254 emergent PCIs (27%) (11). From these data, we infer that in Japan, PCI has been performed primarily based upon anatomical information rather than on physiological evidence of flow-limiting lesions. Thus myocardial perfusion SPECT has not been essential to the justification of PCI. More recently there is increased awareness of the need to demonstrate, prior to intervention, that coronary lesions are flow-limiting (12). However, the results of the Pim et al. study on fractional flow reserve versus angiography for guiding percutaneous coronary intervention (FAME Study) are widely recognized in Japan, so fractional flow reserve is increasingly utilized in preference to myocardial perfusion SPECT to demonstrate the physiological significance of coronary lesions (13).

Similarities between Japan and US

In both countries, despite a high prevalence of CAD and ready accessibility to health care and advanced technology, there has been a significant decline in the number of nuclear cardiology studies performed. According to a recent article by Yoshinaga in the *Journal of Nuclear Cardiology*, in Japan there was a 29% decrease in the number of all (general nuclear medicine and cardiac) SPECT scans performed from 2002 to 2012, and a 19% decrease from 2007 to 2012 (1). In the latter interval, the total number of nuclear cardiology studies declined by 13.7%. The 2015 JROAD survey demonstrated a 3.8% decline in stress myocardial perfusion scans from 203, 568 in 2011 to 195,815 in 2015 (Table 1, 11) despite a 1.0% increase in the number of elective PCI procedures (Fig. 1, 11). In contrast the number of CT coronary angiography (CTA) procedures increased by 21. 9% in parallel to but greatly

Table 1 Cardiac procedures performed in Japan 2011-2015
(From The Japanese Registry of All Cardiac and Vascular Diseases (JROAD): Annual Report 2015 (11) with permission of the Japanese Circulation Society)

	2011	2012	2013	2014	2015
Stress echocardiography	6,009	5,856	5,998	5,915	5,966
Stress MPI	203,586	204,781	204,913	200,889	195,815
Coronary CTA	346,019	360,311	393,872	413,495	421,855
CAG	498,405	504,476	503,776	501,665	498,344
Total PCI	247,994	249,498	253,626	253,370	255,416
Emergent PCI	64,333	67,207	68,749	68,254	69,867
Elective PCI	183,661	181,991	184,877	185,116	185,549
CABG	18,410	18,176	19,345	19,306	18,762

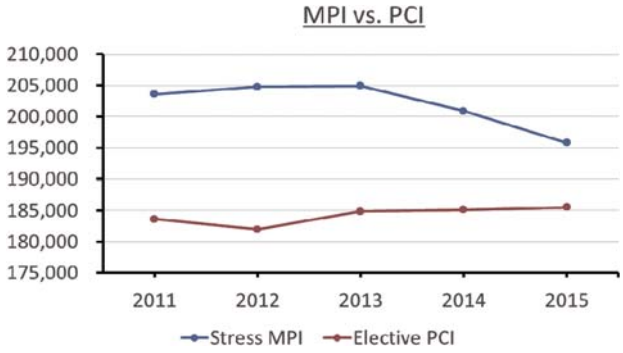

Fig. 1 Number of stress MPI versus PCI procedures performed in Japan 2011-2015 JROAD 2015 Survey (11)
MPI=myocardial perfusion imaging; PCI=percutaneous coronary intervention
(From The Japanese Registry of All Cardiac and Vascular Diseases (JROAD): Annual Report 2015 (11) with permission of the Japanese Circulation Society)

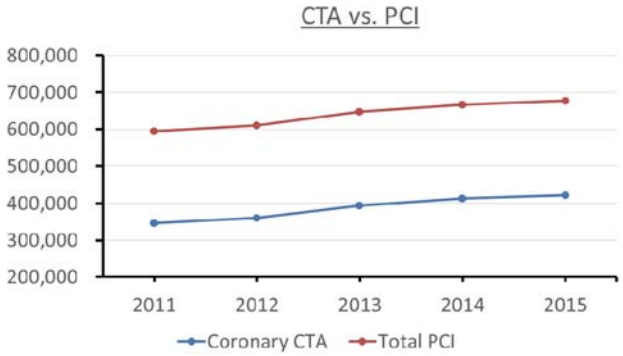

Fig. 2 Number of coronary CTA versus PCI procedures performed in Japan 2011-2015 JROAD 2015 Survey (11)
CTA=computed tomography coronary angiography; PCI=percutaneous coronary intervention
(From The Japanese Registry of All Cardiac and Vascular Diseases (JROAD): Annual Report 2015 (11) with permission of the Japanese Circulation Society)

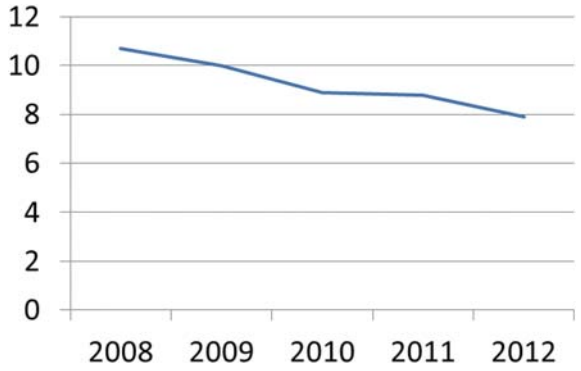

Fig. 3 Ratio of total myocardial perfusion SPECT scans to inpatient consultations and outpatient office visits
SPECT=single-photon emission computed tomography

exceeding the total number of PCIs (Fig. 2, 11). According to an ASNC 2013 survey, from 2008 to 2012 in the US there was a greater than 20% decline in the ratio of myocardial perfusion SPECT scans to the total number of cognitive encounters with cardiology patients (14) (Fig. 3). Thus the US and Japan have experienced a similar progressive decline in nuclear cardiology during the past 5-10 years.

In the US in past years, reimbursement for outpatient procedures was favorable, so many cardiologists incorporated myocardial perfusion imaging into their outpatient office practices. Moreover, patient care was more convenient and expeditious. However, more recently due to reimbursement trends and the fact that private outpatient offices are being acquired by hospitals and more physicians are being employed by hospitals, myocardial perfusion imaging has to some degree shifted back to the hospital setting.

Health care system

American physicians are quite familiar with the challenges of third party insurance coverage, or lack thereof, in the United States for myocardial perfusion SPECT and other nuclear cardiology tests. Implementation of the Affordable Care Act has thankfully expanded health care access to our underserved population. However, there will eventually most likely be an associated decrease in reimbursement for advanced imaging procedures. In Japan all citizens have either government-funded or company-funded health insurance. Nevertheless, according to World Bank statistics, from 2011 to 2015, health care spending constituted 10.3% of Japan's gross domestic

product (GDP), compared to 17.1% in the US. In Japan in recent years, total health care expenditure as a percentage of GDP has declined as has reimbursement to hospitals, probably accounting for the reduction in the use of diagnostic tests including nuclear cardiology tests (1).

Selection of diagnostic tests in the US

Other reasons for the decline in the number of nuclear cardiology studies performed in the two countries are multifold with some similarities and other interesting contrasts. In the United States, we have attributed the decline in the number of nuclear cardiology tests in part to a decline in the incidence of heart disease, thanks to aggressive prevention, diagnosis, and treatment strategies. However, the decline in the use of procedures has also doubtlessly resulted from the burdensome necessity for test precertification. In Japan no precertification for myocardial perfusion SPECT is required. When I was presenting my lecture in Tokyo, I couldn't help but smile when the audience looked puzzled and perplexed as I tried to explain our precertification process. In Japan there are no appropriateness criteria that impact reimbursement policy, and no precertification requirements for expensive cardiac procedures including PCI and coronary artery bypass grafting (CABG). In an internal, unpublished ASNC 2014 test substitution survey, 85% of US respondents indicated that in order to have a myocardial perfusion SPECT scan covered by private health insurance, they were required to secure preauthorization through a radiology business manager (RBM). Fifty-five percent of respondents also indicated that prior authorization was required for Medicare Advantage patients. Over 85% of laboratories indicated that the RBM or payer recommended test substitution. Substituting treadmill exercise testing was recommended in over 70% of such cases, and in approximately 45% of cases, stress echocardiography substitution was recommended. Respondents noted that test substitution was advised with nearly equal frequency whether the patient was asymptomatic or symptomatic and whether the pre-test likelihood of coronary artery disease was low to intermediate or intermediate to high. Over 50% of referring physicians responded that because of precertification requirements, they were less likely to order a myocardial perfusion SPECT study despite meeting appropriate use criteria (15). Nearly 90% of imaging specialists thought that patients were less likely to be referred for nuclear imaging because of precertification requirements.

The emergence of competing modalities such as stress echocardiography and computed tomography coronary angiography (CTA) also likely in part accounts for the decline in nuclear cardiology in the United States. Stress echocardiography is less expensive and more easily accessible than is SPECT, does not require preauthorization, and entails no radiation exposure. The ASNC 2013 survey reported a greater than 30% increase between 2008 and 2012 in the number of outpatient stress echo procedures performed compared to the total number of cardiology office encounters (14) (Fig. 4). As noted above, for patients for whom RBMs or payers recommended test substitution for myocardial perfusion SPECT, the test recommended was stress echocardiography. In contrast, in Japan the use of stress echocardiography is quite limited with only approximately 6,000 procedures performed yearly since 2011 according to the JROAD Survey (11). However, as detailed above, fractional flow reserve has to some degree supplanted myocardial perfusion SPECT in evaluating the hemodynamic consequences of coronary lesions.

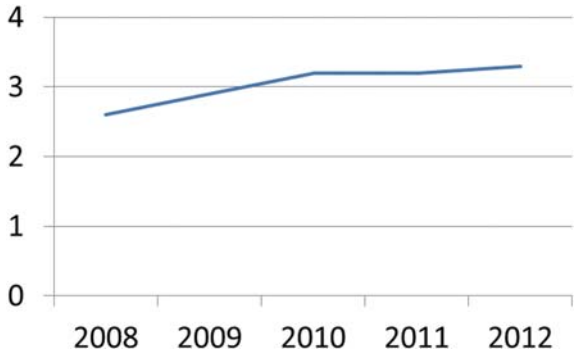

Fig. 4　Ratio of outpatient stress echocardiography procedures to office encounters

Appropriate use of imaging tests

Of course, part of the decline in the number of myocardial perfusion SPECT scans performed in the US is indeed appropriate and has been self-imposed. ASNC, the American College of Radiology (ACR), the ACC, and the SNMMI have all emphasized the need to eliminate nuclear imaging in patients for whom studies are deemed inappropriate (15). The following are some of the guidelines for decreasing the number of inappropriate myocardial perfusion SPECT scans:

- Minimize scans in low-likelihood patients with interpretable electrocardiograms (ECGs) and in asymptomatic non-diabetic patients
- Decrease follow-up scans in patients with initially normal scans (with no change in symptoms)
- Delay/decrease scans in patients following angioplasty and coronary bypass surgery
- Avoid pre-op scans for patients having low-risk surgery

Third party payers are well aware of these recommendations and are ready to deny precertification to patients meeting the above criteria. However, many referring specialists are not fully aware of appropriate use criteria. Confusion and uncertainty result in hesitancy to refer patients to nuclear cardiology as well as denial of precertification. In a 2015

ASNC survey, 54% of respondents were unsure of test necessity, and 40% reported a knowledge gap with regard to the appropriate use criteria (16). The greatest number of inappropriate referrals were identified as coming from nurse practitioners and physician assistants as well as from general practitioners and family physicians. In this survey, it was not clear who was responsible for modifying the inappropriate referral: the imaging specialist, the nuclear technologist, or the referring physician. Similar uncertainty and confusion existed with regard to the individual ultimately responsible for choosing the most appropriate test for the patient.

Yet another reason for the decline in the number of nuclear cardiology studies performed in both the US and Japan is lack of knowledge of the technicalities, protocols, benefits, and limitations of nuclear imaging. This lack of knowledge is shared by both imaging specialists and referring physicians. In the US, certification of both physicians practicing our specialty and laboratories performing nuclear cardiology scans is necessary for third party reimbursement. Presently 1,964 facilities and 3,473 sites are accredited by the International Accreditation Council (IAC) (14). A total of 9,269 physicians are certified by the IAC, including 7,580 cardiologists, 350 nuclear medicine physicians, 1,115 radiologists, and 224 other American Board of Internal Medicine (ABIM) specialists. Other physicians practicing nuclear cardiology are accredited by the American Board of Nuclear Medicine (ABNM) or the ACR. In contrast, in Japan physicians are certified in nuclear medicine, but specific certification in nuclear cardiology is not mandated.

Nevertheless, in the 2015 ASNC survey, 26% of imaging specialists in the United States self-reported a knowledge gap regarding both advances in hardware and software technology and new, emerging radiopharmaceuticals. Referring physicians reported a considerable knowledge gap with regard to the risks and benefits of the various cardiac imaging radiopharmaceuticals and protocols and appropriate use criteria (16) (Table 2). Fifty-three percent of referrals for myocardial perfusion SPECT came from cardiologists, who are usually knowledgeable regarding the indication and benefits of the test; however, the remainder of the referrals came from general/family practitioners and primary care physicians, who may not be as knowledgeable. In Japan, nuclear cardiology is practiced almost exclusively by nuclear medicine physicians. Whereas these physicians are expert in general nuclear medicine, there are gaps in their knowledge of the clinical and technical aspects of nuclear cardiology. Moreover, their ability to report studies meaningfully and to communicate with referring cardiologists may be lacking. For these reasons, further growth and maturation of collaboration with the Japanese Society of Nuclear Cardiology (JSNC) and ASNC has been encouraged. Therefore, our Japanese colleagues are now active participants and contributors in ASNC's International Advisory Panel, and we anticipate a productive collaborative path forward.

Table 2 (16)

Self-reported knowledge gap among referring physicians	
Risks and benefits of ^{99m}Tc in MPI SPECT	28%
Risks and benefits of ^{201}Tl in MPI SPECT	31%
Risks and benefits of ^{82}Rb PET	36%
Risks and benefits of ^{13}N-ammonia PET	44%
Risks and benefits of ^{18}F-FDG PET	44%
New/emerging radiopharmaceuticals	49%
Appropriate Use Criteria	40%

Summary and future directions

In summary, it is interesting and enlightening to learn how two nations with ample resources, active scientific research, and well-trained nuclear physicians differ in their practices of nuclear cardiology. Future collaboration will be fruitful to further this understanding and to promote continued, ongoing research and improvements in clinical care.

Abbreviation and Acronyms

^{123}I-BMIPP: Iodine-123-beta-methyl-p-iodophenylpentadecanoic acid
^{123}I-MIBG: Iodine-123-meta-iodobenzylguanidine
ABIM: American Board of Internal Medicine
ABNM: American Board of Nuclear Medicine
ACR: American College of Radiology
ASNC: American Society of Nuclear Cardiology
CABG: Coronary artery bypass grafting
CT: Computed tomography
CTA: Computed tomography coronary angiography
DPC: Diagnostic procedure combination
DRG: Diagnostic related group
ECG: Electrocardiogram
FAME: Fractional flow reserve versus angiography for guiding percutaneous coronary intervention
GDP: Gross domestic product
IAC: International Accreditation Council
JCS: Japanese Circulation Society
JMHLW: Japanese Ministry of Health, Labor and Welfare
JROAD: Japanese Registry of All Cardiac and Vascular Diseases
MPI: Myocardial perfusion imaging
PCI: Percutaneous coronary intervention
PET: Positron emission tomography
RBM: Radiology business manager
SPECT: Single-photon emission computed tomography

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None

Reprint requests and correspondence:
E. Gordon DePuey, MD
Division of Nuclear Medicine, Department of Radiology Mt. Sinai St. Luke's and Mt. Sinai West Hospitals Icahn School of Medicine at Mt. Sinai New York, NY, USA
E-mail: EDepuey@CHPNET.ORG

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