

ORIGINAL RESEARCH

Worldwide Variation in the Use of Nuclear Cardiology Camera Technology, Reconstruction Software, and Imaging Protocols



Cole B. Hirschfeld, MD,^a Mathew Mercuri, PhD,^{b,c} Thomas N.B. Pascual, MD,^d Ganesan Karthikeyan, MD,^e João V. Vitola, MD, PhD,^f John J. Mahmarian, MD,^g Nathan Better, MD,^h Salah E. Bouyoucef, MD,ⁱ Henry Hee-Seung Bom, MD, PhD,^j Vikram Lele, MD,^k V. Peter C. Magboo, MD,^{l,m} Erick Alexánder, MD,ⁿ Adel H. Allam, MD,^o Mouaz H. Al-Mallah, MD, MS,^g Sharmila Dorbala, MD, MPH,^p Albert Flotats, MD,^q Scott Jerome, DO,^{r,s} Philipp A. Kaufmann, MD,^t Osnat Luxenburg, MD, MPH, MBA,^{u,v} Leslee J. Shaw, PhD,^w S. Richard Underwood, MD,^{x,y} Madan M. Rehani, PhD,^z Diana Paez, MD,^d Maurizio Dondi, MD,^d Andrew J. Einstein, MD, PhD,^{aa,bb} on behalf of the INCAPS Investigators Group

ABSTRACT

OBJECTIVES This study sought to describe worldwide variations in the use of myocardial perfusion imaging hardware, software, and imaging protocols and their impact on radiation effective dose (ED).

BACKGROUND Concerns about long-term effects of ionizing radiation have prompted efforts to identify strategies for dose optimization in myocardial perfusion scintigraphy. Studies have increasingly shown opportunities for dose reduction using newer technologies and optimized protocols.

METHODS Data were submitted voluntarily to the INCAPS (International Atomic Energy Agency Nuclear Cardiology Protocols Study) registry, a multinational, cross-sectional study comprising 7,911 imaging studies from 308 labs in 65 countries. The study compared regional use of camera technologies, advanced post-processing software, and protocol characteristics and analyzed the influence of each factor on ED.

RESULTS Cadmium-zinc-telluride and positron emission tomography (PET) cameras were used in 10% (regional range 0% to 26%) and 6% (regional range 0% to 17%) of studies worldwide. Attenuation correction was used in 26% of cases (range 10% to 57%), and advanced post-processing software was used in 38% of cases (range 26% to 64%). Stress-first single-photon emission computed tomography (SPECT) imaging comprised nearly 20% of cases from all world regions, except North America, where it was used in just 7% of cases. Factors associated with lower ED and odds ratio for achieving radiation dose ≤ 9 mSv included use of cadmium-zinc-telluride, PET, advanced post-processing software, and stress- or rest-only imaging. Overall, 39% of all studies (97% PET and 35% SPECT) were ≤ 9 mSv, while just 6% of all studies (32% PET and 4% SPECT) achieved a dose ≤ 3 mSv.

CONCLUSIONS Newer-technology cameras, advanced software, and stress-only protocols were associated with reduced ED, but worldwide adoption of these practices was generally low and varied significantly between regions. The implementation of dose-optimizing technologies and protocols offers an opportunity to reduce patient radiation exposure across all world regions. (J Am Coll Cardiol Img 2021;14:1819-1828) © 2021 by the American College of Cardiology Foundation.

From the ^aDepartment of Medicine, Columbia University Irving Medical Center/New York-Presbyterian Hospital, New York, New York, USA; ^bDivision of Emergency Medicine, McMaster University, Hamilton, Ontario, Canada; ^cInstitute of Health Policy, Management and Evaluation, Dalla Lana School of Public Health, University of Toronto, Toronto, Ontario, Canada; ^dSection of Nuclear Medicine and Diagnostic Imaging, Division of Human Health, International Atomic Energy Agency, Vienna, Austria; ^eDepartment of Cardiology, All India Institute of Medical Sciences, New Delhi, India; ^fQuanta Diagnóstico and Terapia,

ABBREVIATIONS AND ACRONYMS

ASNC = American Society of Nuclear Cardiology

CAD = coronary artery disease

CT = computed tomography

CZT = cadmium-zinc-telluride

ED = effective dose

MPS = myocardial perfusion scintigraphy

PET = positron emission tomography

SPECT = single-photon emission computed tomography

Tc-99m = technetium-99m

Cardiovascular disease remains a leading cause of worldwide morbidity and mortality, resulting in 17.9 million deaths per year, including 9.4 million from coronary artery disease (CAD) (1). Myocardial perfusion scintigraphy (MPS) is an effective, noninvasive method of diagnosing and risk-stratifying patients with suspected or known CAD. However, MPS is one of the largest contributors to population radiation exposure from medical imaging (2,3).

According to the National Council on Radiation Protection and Measurements, medical imaging was a major driver of rising population radiation dose in recent decades, leading public health authorities to voice concerns over the potential long-term adverse effects of radiation (4-7). This is particularly concerning to cardiology patients, who may require repeat imaging, potentially subjecting them to greater lifetime exposure (8). Proper patient selection and avoidance of unnecessary testing are essential to worldwide dose-reduction efforts, but societal guidelines also propose best practices to facilitate radiological protection during nuclear MPS procedures (9-13). However, a growing body of evidence suggests that individual laboratory adherence to best practices may be lagging (14-17).

Dose optimizing strategies recommended by the American Society of Nuclear Cardiology (ASNC) and the Society of Nuclear Medicine and Molecular

Imaging range from implementing more dose-efficient imaging protocols (e.g., stress-first imaging, avoidance of thallium-201) to installing newer camera technology (e.g., cadmium-zinc-telluride [CZT] or positron emission tomography [PET] cameras) and advanced post-processing software. The extent to which these practices are being used and their impact on radiation exposure across worldwide laboratories remains unknown due to limited available data.

The lack of worldwide and regional data on practice patterns, protocols, and radiation doses in nuclear cardiology led the International Atomic Energy Agency to coordinate a worldwide cross-sectional study of MPS practice, the INCAPS (International Atomic Energy Agency Nuclear Cardiology Protocols Study) registry. Previous INCAPS publications have analyzed variations in regional doses, diagnostic reference levels, and adherence to best practices (14,16,18-23) but have not evaluated specific technologies. In this study, we compare regional use of camera technologies, advanced post-processing software, and imaging protocols and their impact on patient radiation dose.

METHODS

The methods of the INCAPS registry have been previously described (14). In brief, we performed an observational cross-sectional study to identify protocols used for all 7,911 MPS studies conducted at 308 nuclear cardiology laboratories in 65 countries during a single week from March to April 2013. An expert

Curitiba, Brazil; ⁸Department of Cardiology, Houston Methodist DeBakey Heart and Vascular Center, Houston, Texas, USA; ⁹Department of Nuclear Medicine, Royal Melbourne Hospital and University of Melbourne, Melbourne, Australia; ¹⁰Centre Hospitalo-Universitaire de Bab El Oued, Alger, Algeria; ¹¹Department of Nuclear Medicine, Chonnam National University Medical School, Gwangju, Korea; ¹²Department of Nuclear Medicine and PET-CT, Jaslok Hospital and Research Centre, Mumbai, India; ¹³Department of Physical Sciences and Mathematics, University of the Philippines, Manila, the Philippines; ¹⁴Department of Nuclear Medicine, University of Santo Tomas Hospital, Manila, the Philippines; ¹⁵Departamento de Cardiología Nuclear, Instituto Nacional de Cardiología "Ignacio Chávez," Mexico City, Mexico; ¹⁶Cardiology Department, Al Azhar University, Cairo, Egypt; ¹⁷Division of Nuclear Medicine, Department of Radiology, Brigham and Women's Hospital, Boston, Massachusetts, USA; ¹⁸Nuclear Medicine Department, Hospital de la Santa Creu i Sant Pau, Universitat Autònoma de Barcelona, Barcelona, Spain; ¹⁹Intersocietal Accreditation Commission, Ellicott City, Maryland, USA; ²⁰Division of Cardiology, University of Maryland, Baltimore, Maryland, USA; ²¹Department of Nuclear Medicine and Cardiac Imaging, University Hospital Zurich, Zurich, Switzerland; ²²Medical Technology, Health Information and Research Directorate, Ministry of Health, Israel; ²³Israeli Center for Technology Assessment in Health Care, Gertner Institute for Epidemiology and Health Policy Research, Tel Hashomer, Israel; ²⁴New York-Presbyterian/Weill Cornell Medical Center, New York, New York, USA; ²⁵National Heart and Lung Institute, Imperial College London, London, United Kingdom; ²⁶Department of Nuclear Medicine, Royal Brompton and Harefield Hospitals, London, United Kingdom; ²⁷Department of Radiology, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts, USA; ²⁸Seymour, Paul, and Gloria Division of Cardiology, Department of Medicine, Columbia University Irving Medical Center/New York-Presbyterian Hospital, New York, New York, USA; and the ²⁹Department of Radiology, Columbia University Irving Medical Center/New York-Presbyterian Hospital, New York, New York, USA.

James Udelson, MD, served as Guest Editor for this paper.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the [Author Center](#).

committee identified 8 “best practices” relating to radiation exposure. We evaluated the INCAPS registry data for worldwide variability in camera hardware, software technology, and imaging protocols. The study protocol was approved by the Columbia University Institutional Review Board.

DATA COLLECTION. Using a standardized data collection form, each site provided demographic and clinical characteristics for each MPS study during a 1-week period, including age, weight, sex, radiopharmaceutical type and activity injected, camera hardware, patient positioning (e.g., use of prone imaging), type of attenuation correction (AC) scan (computed tomography [CT] or line source) if used, type of camera, and use of advanced post-processing software. Camera types were defined as single head, multiple heads, CZT, or PET. Patient positioning was categorized either single position (supine or prone) or multiple positions (e.g., both supine and prone). Data collected underwent quality control review and site investigators were recontacted to clarify potential omissions, errors, or discrepancies. All sites responded and clarified any discrepancies.

RADIATION DOSE. Radiation dose was quantified as the effective dose (ED) to the patient, a whole body metric that accounts for radiation delivered to each organ with weighting factor applied reflecting the relative sensitivity of each organ to the potentially harmful effects of radiation exposure. ED was calculated for each patient undergoing MPS based on the radiopharmaceutical used and its activity according to dosimetry from the International Commission on Radiological Protection (24). ED was calculated according to the method of Senthamizhchelvan et al. (25) for rubidium-82 PET MPS. The median dose for each site was evaluated for compliance with a target median ED of ≤ 9 mSv, as recommended by professional society guidelines (26).

STATISTICAL ANALYSIS. Continuous variables are summarized as mean \pm SD or median (interquartile range), where appropriate, and compared between groups by analysis of variance or Kruskal-Wallis test, respectively. Categorical variables are compared by chi-square test. Evaluation for independent variables that were associated with ED for MPS was performed by univariable and multivariable linear regression. The variance inflation factor was used to detect multicollinearity between independent variables. Logistic regression was performed for single-photon emission computed tomography (SPECT) MPS for independent variables associated with a binary outcome of ED ≤ 9 mSv. PET, stress-only, and rest-only studies were excluded from this analysis due to

near-perfect prediction of the outcome variable (i.e., almost all these studies were ≤ 9 mSv). A 4-level mixed-effects model was employed for the linear and logistic regressions to account for random effects of clustering at the level of the individual laboratory, country, and region. A 2-tailed p value < 0.05 was considered significant for all statistical tests. All analyses were conducted with Stata/IC 16.1 (StataCorp, College Station, Texas).

RESULTS

A total of 7,911 studies from 308 sites in 65 countries were included. The mean patient age was 64 years and 59% were male. A total of 39% of all studies (97% PET and 35% SPECT) were ≤ 9 mSv, while just 6% of all studies (32% PET and 4% SPECT) achieved a dose ≤ 3 mSv. Overall, there was significant regional variability and low implementation of newer camera technology, advanced post-processing software, and dose-optimizing acquisition protocols (Table 1, Central Illustration).

CAMERA TECHNOLOGY. Regional camera technology data are summarized in Table 1. The most common camera technology was a multiple-head SPECT gamma camera (80%), followed by CZT cameras (10%), PET cameras (6%), and single-head SPECT gamma cameras (4%). The region with highest CZT use was Oceania (26%), followed by Asia (13%), Europe (13%), and North America (8%). No studies utilizing CZT cameras were reported from Latin America or Africa. PET imaging was most prevalent in North America (17%), but represented only 3% of Asian studies and 2% of African and European studies. There were no PET studies reported from Latin America or Oceania. CZT cameras were used in 80% of SPECT studies performed at facilities that reported at least 1 CZT study. Conversely, PET cameras were used in 34% of studies from facilities that reported the use of PET technology (Supplemental Table 1). Additionally, dose-reduced protocols (defined as studies in which the administered activity of at least 1 dose was < 8 mCi, the lower limit for standard-dose protocols) (11) were implemented in 65% of SPECT studies performed with CZT cameras versus 15% of studies using conventional cameras. Use of CZT and PET cameras was associated with reduction in patient radiation exposure for SPECT MPS. Worldwide geographic variability of CZT camera and PET imaging use are illustrated in Figures 1A and 1B, respectively.

RECONSTRUCTION SOFTWARE. Use of AC and use of advanced post-processing software are summarized in Table 1. AC was used in 41% of all facilities and 26%

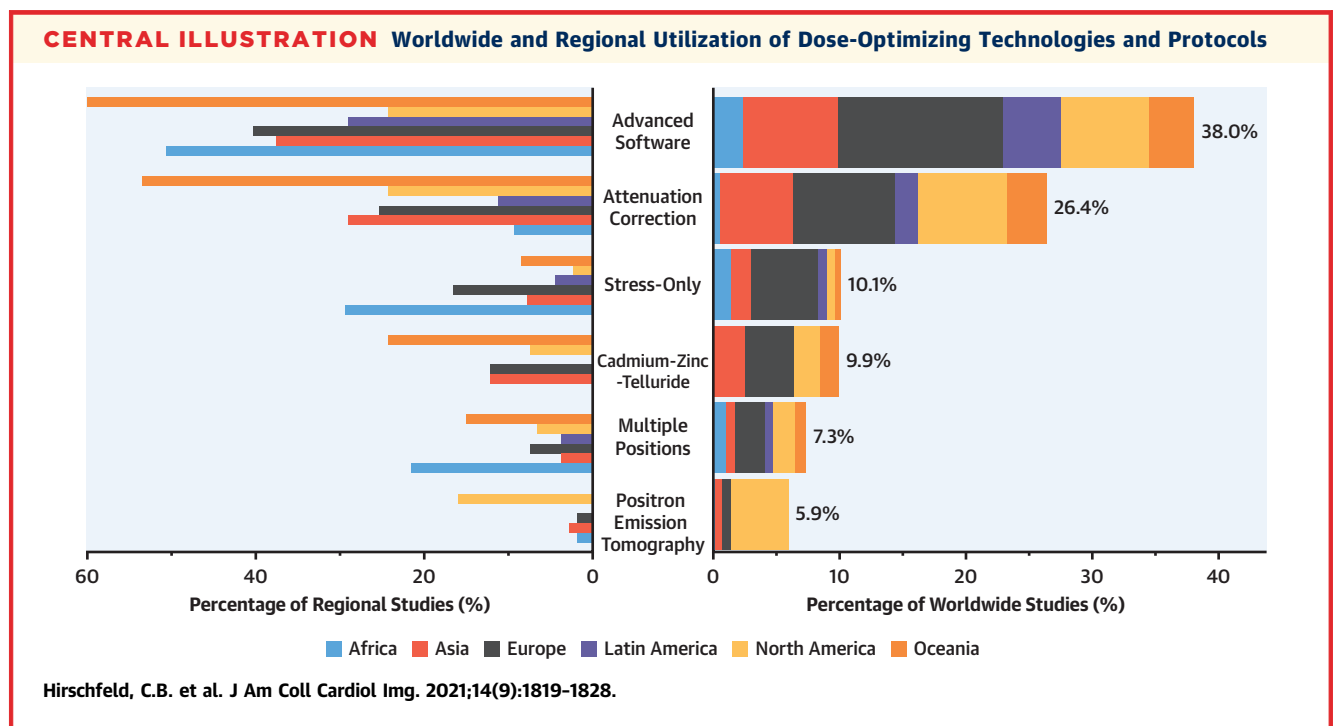
TABLE 1 Comparison of Regional Laboratory Camera Technology, Software, and Imaging Techniques

	Africa (n = 348)	Asia (n = 1,469)	Europe (n = 2,381)	Latin America (n = 1,139)	North America (n = 2,135)	Oceania (n = 439)	Total (N = 7,911)	ED (mSv)
Camera type								
Single head	45 (13)	66 (4)	74 (3)	107 (9)	26 (1)	4 (1)	322 (4)	12.6 ± 4.9
Multiple heads	297 (85)	1,156 (79)	1,943 (82)	1,032 (91)	1,583 (74)	322 (73)	6,333 (80)	10.6 ± 4.2
CZT	–	194 (13)	312 (13)	–	163 (8)	113 (26)	782 (10)	7.1 ± 3.2
PET	6 (2)	53 (4)	52 (2)	–	363 (17)	–	474 (6)	3.7 ± 2.4
Patient position								
Single position	267 (77)	1,415 (96)	2,195 (92)	1,090 (96)	1,996 (93)	370 (84)	7,333 (93)	9.9 ± 4.5
Multiple position	81 (23)	54 (4)	186 (8)	49 (4)	139 (7)	69 (16)	578 (7)	10.2 ± 4.0
Attenuation correction								
Without AC	312 (90)	1,007 (69)	1,743 (73)	1,000 (88)	1,574 (74)	190 (43)	5,826 (74)	10.3 ± 4.4
With AC	36 (10)	462 (31)	638 (27)	139 (12)	561 (26)	249 (57)	2,085 (26)	9.0 ± 4.6
Software								
Standard	161 (46)	877 (60)	1,347 (57)	781 (69)	1,580 (74)	159 (36)	4,905 (62)	10.0 ± 4.7
Advanced	187 (54)	592 (40)	1,034 (43)	358 (31)	555 (26)	280 (64)	3,006 (38)	9.9 ± 4.1

Values are n (%) or mean ± SD.
AC = attenuation correction; CZT = cadmium-zinc-telluride; ED = effective dose; PET = positron emission tomography.

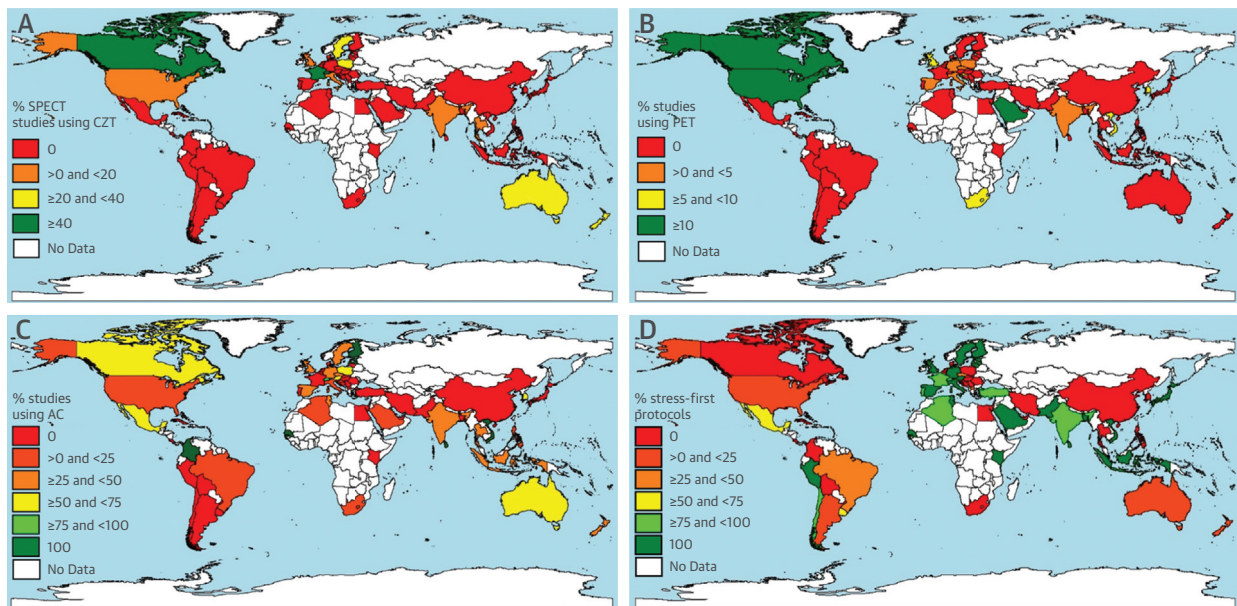
of all cases worldwide. The highest proportion was observed in Oceania (57%), followed by Asia (31%), Europe (27%), North America (26%), Latin America (12%), and Africa (10%). Studies employing AC had decreased radiation exposure compared with those

with no AC (9.0 mSv vs. 10.3 mSv; $p < 0.001$). This difference was driven by a significantly lower ED with CT AC compared with line source AC (8.9 mSv vs. 10.4 mSv; $p < 0.001$) (Supplemental Table 2). Furthermore, the proportion of stress-only studies was greater for



Graphs displaying the percentage of worldwide (right) and regional (left) studies employing newer-technology cameras, software, and advanced imaging techniques. The stacked bars (right) show the regional proportions for all worldwide studies, whereas the clustered bars (left) show the proportion of regional studies employing each dose-optimizing practice. Advanced software and attenuation correction were used most frequently, while use of stress-only protocols, cadmium-zinc-telluride (CZT) cameras, multiple positions, and positron emission tomography (PET) cameras were less common.

FIGURE 1 Geographic Variability of Technology and Protocol Utilization Around the World



World maps demonstrating the percentage of studies in each country utilizing (A) cadmium-zinc-telluride (CZT) cameras, (B) positron emission tomography (PET) cameras, (C) attenuation correction imaging, and (D) stress-first imaging protocols. The use of dose-optimizing technologies and protocols was generally low and varied greatly between world regions and countries. AC = attenuation correction; SPECT = single-photon emission computed tomography.

technetium (Tc)-99m-based stress-first protocols utilizing CT AC (27%) versus line source AC (20%) or no AC (22%). Advanced post-processing software was used in 38% of sites and was also associated with both decreased estimated radiation dose and increased likelihood of achieving ED ≤ 9 mSv. **Figure 1C** illustrates geographic variability in the use of AC.

IMAGING PROTOCOLS. **Table 2** summarizes the breakdown of regional imaging protocols. Significant variations in protocol use were observed between world regions. Stress-only imaging was used most frequently in Africa (32%) and Europe (18%). Stress-first SPECT imaging comprised nearly 20% of cases from all world regions except North America, where it was used in just 7% of cases. Rest-stress imaging was used in 90% of North American cases and 73% of Oceanic cases compared with only 14% of European cases. Tc-99m-labeled radiotracers were used in more than 93% of SPECT studies from every region except Asia, where 20% of studies were thallium-201 or dual-isotope protocols. **Figure 1D** demonstrates the geographic variability of stress-first imaging protocols. Images from 578 studies were acquired using multiple patient positions. While multiple positions was not associated with decreased ED in our study population, the proportion of stress-only studies was

55% higher among stress-first protocols employing multiple positions (31% vs. 20%; $p < 0.001$). PET studies were used infrequently, comprising fewer than 5% of studies from every region except North America (17%).

LINEAR REGRESSION AND LOGISTIC REGRESSION.

Multivariable linear regression results are summarized in **Table 3** and multivariable logistic regression results are displayed in **Figure 2**. PET cameras, CZT cameras, stress-only and rest-only protocols, and advanced software were associated with lower ED for SPECT MPS in a multivariable model. CZT camera (odds ratio: 26.1; 95% confidence interval: 12.7 to 53.5; $p < 0.001$) and advanced software (odds ratio: 5.5; 95% confidence interval: 3.0 to 10.0; $p < 0.001$) were associated with associated with ED ≤ 9 mSv.

DISCUSSION

Using data from the worldwide INCAPS registry, we examined variations among regional technology use and protocols for MPS and analyzed characteristics associated with patient radiation dose. In our cohort, 39% of all MPS studies achieved a dose of ≤ 9 mSv, while just 6% achieved a dose ≤ 3 mSv. Factors associated with reduced radiation dose during MPS

TABLE 2 Distribution of Regional Study Protocols and Effective Doses

Protocol	Africa	Asia	Europe	Latin America	North America	Oceania	Total	Mean ED (mSv)	Median ED (mSv)
1-day SPECT	175	1,121	1,455	654	1,661	402	5,468	10.0 ± 4.4	10.9 (6.8-12.5)
Tc-99m									
Stress only	109	122	421	53	52	40	797	3.9 ± 1.7	3.4 (2.7-5.1)
Rest only	6	43	133	81	12	3	278	5.0 ± 1.7	4.9 (3.5-6.0)
Stress-rest	48	373	776	199	22	43	1,461	9.7 ± 2.9	9.6 (7.8-11.4)
Rest-stress	10	293	59	296	1,549	284	2,491	11.4 ± 2.7	11.6 (9.9-12.8)
Dual isotope	—	105	6	11	24	—	146	21.2 ± 3.0	21.6 (19.9-22.8)
Tl-201, 1 injection	—	166	39	1	2	17	225	14.5 ± 2.6	15.5 (12.5-16.4)
Tl-201, 2 injections	—	19	21	13	—	5	58	18.4 ± 3.4	19.2 (16.8-20.7)
Other 1-day SPECT	2	—	—	—	—	10	12	13.7 ± 3.0	13.6 (11.3-15.7)
Multiday SPECT	167	295	874	485	111	37	1,969	11.4 ± 3.9	11.3 (8.8-14.0)
Tc-99m stress-rest	145	238	599	166	57	2	1,207	11.6 ± 3.7	11.2 (9.1-14.1)
Tc-99m rest-stress	22	49	271	317	52	35	746	11.0 ± 3.8	9.9 (8.3-13.8)
Other multiday SPECT	—	8	4	2	2	—	16	19.1 ± 8.4	20.7 (14.3-20.7)
PET	6	53	52	—	363	—	474	3.7 ± 2.5	3.6 (2.5-4.0)
FDG viability study	6	17	9	—	11	—	43	9.2 ± 5.2	7.5 (4.9-11.7)
Rb-82 rest-stress	—	11	30	—	339	—	380	3.3 ± 0.8	3.5 (2.7-3.9)
N-13 NH ₃ rest/stress	—	19	7	—	10	—	36	2.8 ± 1.2	2.9 (1.7-3.3)
Other PET	—	6	6	—	3	—	15	1.5 ± 0.5	1.2 (1.1-2.3)
Total	348	1,469	2,381	1,139	2,135	439	7,911	10.0	

Values are n, mean ± SD, or median (interquartile range).
FDG = fluorodeoxyglucose; Rb-82 = rubidium-82; SPECT = single-photon emission computed tomography; Tc-99m = technetium-99m; Tl-201 = thallium-201; other abbreviations as in Table 1.

included use of newer technology cameras, use of advanced post-processing software, and protocol used (e.g., stress-only imaging). These same factors were also statistically associated with a total patient radiation dose ≤ 9 mSv. We observed significant variability in regional practices, protocols, and use of advanced software and camera technology, highlighting the need for further implementation of dose-optimizing practices and standardization of international protocols to improve dose-reduction efforts in all world regions.

In general, newer camera technologies, such as CZT or PET, enable MPS studies to be performed with significantly reduced radiation dose when compared with conventional SPECT cameras. The greater sensitivity and efficiency of CZT cameras over conventional gamma cameras allows for high-resolution MPS with reduced administered activity, resulting in reduced radiation dose. Duvall et al. (27) showed that laboratories utilizing CZT cameras in combination with dose-reduced protocols could potentially achieve a dose reduction of 50% compared with conventional Tc-99m dosing and up to 75% compared with dual-isotope protocols. The 2016 ASNC Stress Protocols and Tracers guidelines distinguish dosing for protocols based on camera technology, reducing the recommended administered activity for a scan by about 50% for newer technology cameras. For example, the total recommended administered activity for a Tc-99m 2-day stress-rest protocol with a conventional SPECT gamma camera is listed as 16 to 24 mCi, whereas the activity recommended for newer technology cameras is only 8 to 12mCi (11). Our data also showed that SPECT studies utilizing CZT cameras were more likely to use dose-reduced protocols, were correlated with lower ED, and were significantly more likely to achieve an ED ≤ 9 mSv. Studies employing CZT cameras saw a reduction in mean ED of 44% when compared with single-head gamma cameras (7.1 mSv vs. 12.6 mSv;

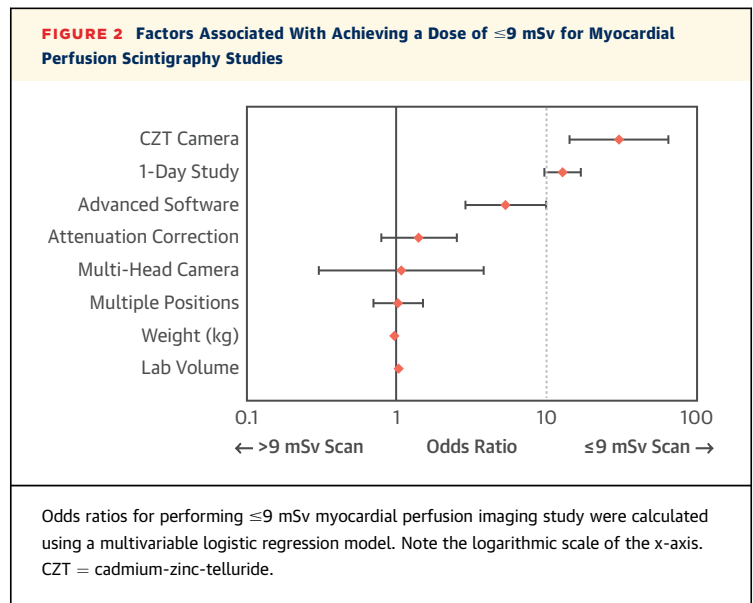
TABLE 3 Factors With Statistically Significant Correlation to ED for SPECT Myocardial Perfusion Scintigraphy Based on a Multivariable Linear Regression Analysis

Variables Associated With ED	Beta	SE	95% CI		p Value
			Lower	Upper	
PET camera	-7.17	0.15	-7.47	-6.88	<0.001
CZT camera	-2.81	0.16	-3.12	-2.50	<0.001
Stress only	-6.14	0.08	-6.29	-5.99	<0.001
Rest only	-5.48	0.12	-5.71	-5.25	<0.001
Advanced software	-1.12	0.13	-1.37	-0.88	<0.001
Thallium scan	4.96	0.15	4.66	5.26	<0.001
Dual isotope	7.17	0.25	6.67	7.67	<0.001
AC	0.35	0.13	0.10	0.60	0.006
Weight	0.04	0.00	0.03	0.04	<0.001
Lab volume	-0.01	0.00	-0.02	0.00	0.015

CI = confidence interval; other abbreviations as in Tables 1 and 2.

$p < 0.001$) and 33% compared with multihead gamma cameras (7.1 mSv vs. 10.6 mSv; $p < 0.001$). Despite this, use of CZT cameras was low in all world regions (range 0% to 26%), likely owing in large part to the substantial upfront cost of this technology.

PET imaging is also associated with significantly lower ED than SPECT MPS, with a mean ED of 3.7 mSv versus 10.4 mSv in our analysis. Desiderio et al. (17) analyzed 532 PET studies from 111 U.S. laboratories and similarly found that mean ED was 3.7 mSv, with 100% of PET studies using a dose ≤ 9 mSv compared with just 2.6% of reported SPECT studies. Despite substantial radiation reductions with PET technology, use of PET imaging was also low, at just 6% of studies worldwide (range 0% to 17%), which may be due to cost-prohibitive factors, as well as to the lack of availability of cardiac PET tracers in many countries, including high-income countries such as Australia. Additionally, the unwillingness of third-party payers to reimburse for the procedure may contribute to lower use in some regions, especially North America. Not only are the acquisition and maintenance costs of PET cameras pricier than conventional SPECT cameras, but the radiotracer itself requires a portable generator for ^{82}Rb or an onsite or nearby cyclotron for $^{13}\text{N-NH}_3$ or $^{15}\text{O-H}_2\text{O}$, further raising the total cost of ownership (28,29). Some studies have shown that the use of PET MPS might actually reduce downstream costs associated with cardiac revascularization. Merhige et al. (29) reported that use of PET MPS in patients with intermediate risk of CAD reduced rates of cardiac catheterization by more than 50% at 1 year while reducing costs by up to 30% when compared with conventional SPECT MPS. However, a more recent study analyzing >15,000 MPS studies performed at a single hospital in Utah showed that a greater proportion of all patients evaluated with PET MPS underwent coronary angiography compared with those evaluated with SPECT MPS (13.2% vs 9.7%; $p < 0.0001$) (30). The authors also report that PET MPS improved identification of high-grade CAD and led to significantly more revascularizations in patients undergoing coronary angiography compared with SPECT MPS. The availability of perfusion radiotracers that can be obtained as a unit dose without expensive on-site equipment, such as $^{18}\text{F-flurpiridaz}$, could also help to reduce cost and make PET cameras a more economical choice for cardiology imaging laboratories around the world. Desiderio et al. (17) reported a 4-fold increase in applications for PET accreditation to the Intersocietal Accreditation Commission from 2012 to 2015, suggesting that the availability and use of PET MPS in the United States is likely to be greater today (17). Furthermore, guidelines have increasingly provided



updated information on the use of PET MPS. Where available, PET imaging offers a substantial opportunity to achieve a total patient dose of ≤ 9 mSv in a majority of MPS studies.

Additional factors associated with reduced ED were the use of advanced post-processing software, though the effect size was small in our sample. We believe that this could indicate that laboratories were more likely to use this technology to reduce image acquisition time rather than patient radiation exposure. Al Badarin et al. (31) evaluated factors affecting radiation dose in an analysis of nearly 56,000 MPS studies in a large Midwestern U.S. health system and found that Tc-99m stress-only studies employing advanced post-processing software with conventional cameras were associated with a dose reduction of 10.1 mSv over conventional rest-stress studies, compared with 6.0 mSv for stress-only studies that did not use advanced post-processing software. One concern with low-dose stress-first protocols is the potential for inferior image quality, which could lead to greater uncertainty interpreting results and potentially increase downstream costs and radiation exposure through the need for additional testing. However, mounting evidence continues to show that high-efficiency cameras and advanced software enable studies to be performed with lower administered activities while maintaining image quality (11,32,33). For example, DePuey et al. (32) demonstrated that very low-dose stress-first protocols performed on sodium-iodide SPECT cameras with administered activity of just 5 mCi (approximately 1.4-mSv dose) can provide adequate image quality with the use of advanced post-processing

software. Advancements in nuclear MPS software, including resolution recovery, noise reduction, and iterative reconstruction, allow for much lower administered activity, yet they remain underutilized in most world regions (34).

AC was also associated with lower ED in our study (9.0 mSv vs. 10.3 mSv). Interestingly, compared with line source AC, studies utilizing CT AC saw greater reductions in ED. This could be because stress-first protocols performed with CT AC achieved a higher proportion of stress-only studies. Despite its advantages, AC was also underutilized, with reported use in only one-quarter of worldwide studies. Thus, there remains significant potential worldwide to realize greater dose optimization with increased use of AC.

Where AC and advanced post-processing software is unavailable, another dose-reduction technique that requires no financial investment is the use of multiple patient positions. Usually this takes the form of prone imaging as well as supine, although for some cameras it constitutes seated as well as supine imaging. Updated guidelines indicate that the addition of prone positioning may help distinguish attenuation artifact from potential perfusion defects, thereby reducing the rate of false positive studies (35,36). A study of 279 patients who underwent both prone and supine imaging reported that prone positioning reversed 40% of scans from potentially abnormal to normal or probably normal (36). Hence, the use of multiple positions in stress-first protocols should increase the number of stress-only studies, thereby reducing radiation exposure. Multiple-position imaging was performed in just 7% of cases in our cohort. When analyzing all studies together, we did not observe a significant difference in patient dose between single- and multiple-position image acquisition (9.9 mSv vs. 10.2 mSv), though this study was not specifically designed to analyze this factor. However, we found that the proportion of stress-only studies was significantly greater for stress-first protocols employing multiple positions than for stress-first protocols with only 1 position, suggesting that multiple-position imaging can obviate the need for subsequent rest imaging in many patients.

We also re-evaluated other well-established best practices for dose optimization that have been reported previously, such as avoidance of thallium and dual-isotope studies. The mean worldwide ED of SPECT studies using thallium or dual isotope protocols was 17.3 mSv versus 9.9 mSv for protocols using only Tc-99m. Despite greater radiation exposure, 6.1% of SPECT studies worldwide still used thallium-based protocols, with the greatest burden seen in Asia, where thallium was used in 20% of reported

SPECT protocols. Although just 2% of U.S. SPECT studies used thallium or dual-isotope protocols in our study, separate reports of Intersocietal Accreditation Commission accreditation data from 2012 to 2015 by Jerome et al. (15) and Desiderio et al. (17) showed that these protocols were used in 8% to 9% of submitted studies, rates that remained stable over the 4-year period despite guidelines recommending the avoidance of thallium when possible. Continued attention to reducing the use of thallium will lower patient radiation exposure and increase the likelihood of achieving a patient radiation dose ≤ 9 mSv (14).

Finally, the use of stress-first protocols was notably lower in the United States (7%) compared with other world regions (range 19% to 88%). The ASNC published updated guidelines in 2018 strongly recommending the use of stress-first imaging where feasible, given the potential to avoid subsequent rest imaging and reduce patient radiation exposure (37). Current remuneration schemes in numerous countries (e.g., the United States and Brazil) may dissuade facilities from performing single studies (e.g., stress only) due to greater reimbursement for multiple studies (e.g., stress-rest) (38). However, equalization of reimbursements could also inappropriately incentivize facilities to avoid rest imaging when it is needed. For example, when the presence of attenuation artifact, which is particularly problematic for obese patients, might interfere with image interpretation or for patients with prior myocardial infarction in which stress-only imaging may not be applicable. Nevertheless, many present reimbursement systems provide strong disincentives for laboratories to consider stress-only imaging in the patients for whom it is warranted. Development of more equitable systems are needed to increase use of stress-only imaging and decrease radiation exposure to populations.

STUDY LIMITATIONS. These findings must be interpreted in the context of inherent study limitations. The INCAPS registry was an observational study in which data were collected from each facility during a single week, and national and regional participation in the study was variable. Thus, the extent to which these data represent the complete distribution of studies performed at an individual laboratory, country, or region is unknown. However, the INCAPS registry is one of the largest registries of MPS studies and represents the first regional data available in several world regions. Additionally, the study design is prone to potential sampling bias (e.g., a facility that participated in an online survey could conceivably be more technologically advanced than non-participants), which might result in overestimating

the use of newer technologies in some regions. However, results from prior INCAPS studies and the findings published here, where comparable, are generally in agreement with previously published data (16,18-21). Furthermore, our results do not account for the influence of radiation differences on study acquisition time or image quality; however, prior research exists to address the association of these study characteristics with radiation dose (33,34). Finally, it is important to note that all reported EDs are estimates based on both measured quantities and standardized assumptions. Nonetheless, ED is a standard metric quantifying radiation to the whole body that is used across diverse medical applications, and was useful in analyzing regional protocols and technologies in this study.

We also recognize that since the INCAPS implementation, which was carried out in 2013, updated guidelines have been published, and changes in hardware, software, and clinical protocols have been put into effect in many facilities worldwide. While it seems unlikely that there has been marked growth in the use of new technologies such as CZT and PET, this remains to be demonstrated. In view of this, the International Atomic Energy Agency will lead the implementation of INCAPS 2 beginning in 2021, which is expected to provide updated data on global technology, acquisition protocols, and dosing trends for MPS.

CONCLUSIONS

In this study, we observed that newer-technology cameras, advanced software, and stress-only protocols were associated with reduced ED. Nevertheless, regional use of these dose-optimizing practices varied and was generally low, signifying major opportunities to reduce patient radiation exposure across the globe. Patient radiation exposure from MPS will continue to improve through adherence to best practices and the implementation of advanced technologies and dose-optimizing protocols.

ACKNOWLEDGEMENTS The authors thank the members of the INCAPS Investigators Group (Supplemental Appendix), and their institutions, for efforts in collecting data, and the cooperating professional societies, including the American Society of

Nuclear Cardiology, Asian Regional Cooperative Council for Nuclear Medicine, Australian and New Zealand Society of Nuclear Medicine, British Nuclear Medicine Society/British Nuclear Cardiology Society, Comissão Nacional de Energia Nuclear, European Association of Nuclear Medicine, European Council of Nuclear Cardiology, International Atomic Energy Agency, and Intersocietal Accreditation Commission.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

This work was supported by the International Atomic Energy Agency, the Margaret Q. Landenberger Research Foundation (in memory of Prof. A. Donny Strosberg), and the Irving Scholars Program (to Dr. Einstein). Dr. Einstein has served as a consultant to W.L. Gore and Associates; has received an honorarium for lecturing from Ionetix; has received institutional research grants from the National Institutes of Health, International Atomic Energy Agency, Canon Medical Systems, GE Healthcare, Roche Medical Systems, and W.L. Gore and Associates; and has received travel expenses unrelated to activities listed from HeartFlow. Dr. Kaufmann has received institutional research grant support from GE Healthcare. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

ADDRESS FOR CORRESPONDENCE: Dr. Andrew J. Einstein, Columbia University Irving Medical Center, Seymour, Paul, and Gloria Milstein Division of Cardiology, 622 West 168th Street, PH 10-203, New York, New York 10032, USA. E-mail: andrew.einstein@columbia.edu. Twitter: [@AndrewEinstein7](https://twitter.com/AndrewEinstein7).

PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: This is the first study to evaluate worldwide differences in technologies and protocols for MPS. Despite significant reductions in ED with CZT and PET cameras, advanced software, and stress-only protocols, use of these dose-optimizing practices was generally low and varied greatly between world regions.

TRANSLATIONAL OUTLOOK: Dose-optimizing technologies and protocols are used infrequently and inconsistently in all world regions, signaling major opportunities to reduce patient radiation exposure. Ongoing surveillance of regional practices is imperative to continued efforts to improve radiological protection around the world.

REFERENCES

1. World Health Organization. *Global Health Estimates 2016: Deaths by Cause, Age, Sex, by Country and by Region, 2000-2016* 2020. Geneva, Switzerland: World Health Organization; 2020. http://www.who.int/healthinfo/global_burden_disease/estimates/en/. Accessed July 2, 2020.
2. Einstein AJ. Effects of radiation exposure from cardiac imaging: how good are the data? *J Am Coll Cardiol*. 2012;59:553-565.

3. Fazel R, Krumholz HM, Wang Y, et al. Exposure to low-dose ionizing radiation from medical imaging procedures. *N Engl J Med*. 2009;361:849-857.
4. Einstein AJ, Tilkemeier P, Fazel R, Rakotoarivelo H, Shaw LJ. American Society of Nuclear Cardiology. Radiation safety in nuclear cardiology—current knowledge and practice: results from the 2011 American Society of Nuclear Cardiology member survey. *JAMA Intern Med*. 2013;173:1021-1023.
5. Shaw LJ, Marwick TH, Zoghbi WA, et al. Why all the focus on cardiac imaging? *J Am Coll Cardiol Img*. 2010;3:789-794.
6. Schauer DA, Linton OW. National Council on Radiation Protection and Measurements report shows substantial medical exposure increase. *Radiology*. 2009;253:293-296.
7. National Council on Radiation Protection and Measurements. *Reference Levels and Achievable Doses in Medical and Dental Imaging: Recommendations for the United States. NCRP Report No. 172*. Bethesda, MD: National Council on Radiation Protection and Measurements; 2012.
8. Chen J, Einstein AJ, Fazel R, et al. Cumulative exposure to ionizing radiation from diagnostic and therapeutic cardiac imaging procedures: a population-based analysis. *J Am Coll Cardiol*. 2010;56:702-711.
9. American College of Radiology. *Practice Guidelines and Technical Standards*. Reston, VA: American College of Radiology; 2008.
10. Dorbala S, Di Carli MF, Delbeke D, et al. SNMMI/ASNC/SCCT guideline for cardiac SPECT/CT and PET/CT 1.0. *J Nucl Med*. 2013;54:1485-1507.
11. Henzlova MJ, Duvall WL, Einstein AJ, Travin MI, Verberne HJ. ASNC imaging guidelines for SPECT nuclear cardiology procedures: stress, protocols, and tracers. *J Nucl Cardiol*. 2016;23:606-639.
12. Hirshfeld JW Jr., Ferrari VA, Bengel FM, et al. 2018 ACC/HRS/NASCI/SCAI/SCCT expert consensus document on optimal use of ionizing radiation in cardiovascular imaging: best practices for safety and effectiveness: a report of the American College of Cardiology Task Force on Expert Consensus Decision Pathways. *J Am Coll Cardiol*. 2018;71:e283-e351.
13. Vano E, Miller DL, Martin CJ, et al. ICRP publication 135: diagnostic reference levels in medical imaging. *Ann ICRP*. 2017;46:1-144.
14. Einstein AJ, Pascual TN, Mercuri M, et al. Current worldwide nuclear cardiology practices and radiation exposure: results from the 65 country IAEA Nuclear Cardiology Protocols Cross-Sectional Study (INCAPS). *Eur Heart J*. 2015;36:1689-1696.
15. Jerome SD, Tilkemeier PL, Farrell MB, Shaw LJ. Nationwide Laboratory Adherence to Myocardial Perfusion Imaging Radiation Dose Reduction Practices: a report from the Intersocietal Accreditation Commission Data Repository. *J Am Coll Cardiol Img*. 2015;8:1170-1176.
16. Mercuri M, Pascual TN, Mahmarian JJ, et al. Comparison of radiation doses and best-practice use for myocardial perfusion imaging in US and non-US laboratories: findings from the IAEA (International Atomic Energy Agency) Nuclear Cardiology Protocols Study. *JAMA Intern Med*. 2016;176:266-269.
17. Desiderio MC, Lundbye JB, Baker WL, Farrell MB, Jerome SD, Heller GV. Current status of patient radiation exposure of cardiac positron emission tomography and single-photon emission computed tomographic myocardial perfusion imaging. *Circ Cardiovasc Imaging*. 2018;11:e007565.
18. Biswas S, Better N, Pascual TN, et al. Nuclear cardiology practices and radiation exposure in the Oceania region: results from the IAEA Nuclear Cardiology Protocols Study (INCAPS). *Heart Lung Circ*. 2017;26:25-34.
19. Lindner O, Pascual TN, Mercuri M, et al. Nuclear cardiology practice and associated radiation doses in Europe: results of the IAEA Nuclear Cardiology Protocols Study (INCAPS) for the 27 European countries. *Eur J Nucl Med Mol Imaging*. 2016;43:718-728.
20. Pascual TN, Mercuri M, El-Haj N, et al. Nuclear cardiology practice in Asia: analysis of radiation exposure and best practice for myocardial perfusion imaging—results from the IAEA Nuclear Cardiology Protocols Cross-Sectional Study (INCAPS). *Circ J*. 2017;81:501-510.
21. Vitola JV, Mut F, Alexanderson E, et al. Opportunities for improvement on current nuclear cardiology practices and radiation exposure in Latin America: Findings from the 65-country IAEA Nuclear Cardiology Protocols cross-sectional Study (INCAPS). *J Nucl Cardiol*. 2017;24:851-859.
22. Hirschfeld CB, Dondi M, Pascual TNB, et al. Worldwide diagnostic reference levels for single-photon emission computed tomography myocardial perfusion imaging: findings from INCAPS. *J Am Coll Cardiol Img*. 2021;14(3):657-665.
23. Shi L, Dorbala S, Paez D, et al. Gender differences in radiation dose from nuclear cardiology studies across the world: findings from the INCAPS registry. *J Am Coll Cardiol Img*. 2016;9:376-384.
24. Cousins C, Miller D, Bernardi G, et al. ICRP publication 120: radiological protection in cardiology. *Ann ICRP*. 2013;42:1-125.
25. Senthamizhchelvan S, Bravo PE, Esaias C, et al. Human biodistribution and radiation dosimetry of ⁸²Rb. *J Nucl Med*. 2010;51:1592-1599.
26. Cerqueira MD, Allman KC, Ficaro EP, et al. Recommendations for reducing radiation exposure in myocardial perfusion imaging. *J Nucl Cardiol*. 2010;17:709-718.
27. Duvall WL, Croft LB, Ginsberg ES, et al. Reduced isotope dose and imaging time with a high-efficiency CZT SPECT camera. *J Nucl Cardiol*. 2011;18:847-857.
28. Ghotbi AA, Kjaer A, Hasbak P. Review: comparison of PET rubidium-82 with conventional SPECT myocardial perfusion imaging. *Clin Physiol Funct Imaging*. 2014;34:163-170.
29. Merhige ME, Breen WJ, Shelton V, Houston T, D'Arcy BJ, Perna AF. Impact of myocardial perfusion imaging with PET and ⁸²Rb on downstream invasive procedure utilization, costs, and outcomes in coronary disease management. *J Nucl Med*. 2007;48:1069-1076.
30. Knight S, Min DB, Le VT, et al. Implementation of a cardiac PET stress program: comparison of outcomes to the preceding SPECT era. *JCI Insight*. 2018;3:e120949.
31. Al Badarin FJ, Spertus JA, Bateman TM, et al. Drivers of radiation dose reduction with myocardial perfusion imaging: a large health system experience. *J Nucl Cardiol*. 2019;27:785-794.
32. DePuey EG, Ata P, Wray R, Friedman M. Very low-activity stress/high-activity rest, single-day myocardial perfusion SPECT with a conventional sodium iodide camera and wide beam reconstruction processing. *J Nucl Cardiol*. 2012;19:931-944.
33. Einstein AJ, Blankstein R, Andrews H, et al. Comparison of image quality, myocardial perfusion, and left ventricular function between standard imaging and single-injection ultra-low-dose imaging using a high-efficiency SPECT camera: the MILLISIEVERT study. *J Nucl Med*. 2014;55:1430-1437.
34. Slomka PJ, Dey D, Duvall WL, Henzlova MJ, Berman DS, Germano G. Advances in nuclear cardiac instrumentation with a view towards reduced radiation exposure. *Curr Cardiol Rep*. 2012;14:208-216.
35. Abbott BG, Case JA, Dorbala S, et al. Contemporary Cardiac SPECT Imaging-Innovations and Best Practices: an information statement from the American Society of Nuclear Cardiology. *J Nucl Cardiol*. 2018;25:1847-1860.
36. Guner LA, Caliskan B, Isik I, Aksoy T, Vardareli E, Parspur A. Evaluating the role of routine prone acquisition on visual evaluation of SPECT images. *J Nucl Med Technol*. 2015;43:282-288.
37. Dorbala S, Ananthasubramaniam K, Armstrong IS, et al. Single photon emission computed tomography (SPECT) myocardial perfusion imaging guidelines: instrumentation, acquisition, processing, and interpretation. *J Nucl Cardiol*. 2018;25:1784-1846.
38. Centers for Medicare and Medicaid Services. Medicare Program: Changes to Hospital Outpatient Prospective Payment and Ambulatory Surgical Center Payment Systems and Quality Reporting Programs; Revisions of Organ Procurement Organizations Conditions of Coverage Prior Authorization Process and Requirements for Certain Covered Outpatient Department Services; Potential Changes to the Laboratory Date of Service Policy; Changes to Grandfathered Children's Hospitals-Within-Hospitals; Notice of Closure of Two Teaching Hospitals and Opportunity To Apply for Available Slots; Correction. *Fed Regist*. 2020;85:224-230.

KEY WORDS camera technology, myocardial perfusion scintigraphy, nuclear cardiology protocols, radiation dose reduction, SPECT

APPENDIX For supplemental tables, please see the online version of this paper.