Worldwide Variation in the Use of Nuclear Cardiology Camera Technology, Reconstruction Software, and Imaging Protocols: Findings from the IAEA Nuclear Cardiology Protocols Study (INCAPS)

Brief title: Nuclear Cardiology Technology and Protocols

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STRUCTURED ABSTRACT

Background: Concerns about long-term effects of ionizing radiation have prompted efforts to identify strategies for dose optimization in myocardial perfusion scintigraphy (MPS). Studies have increasingly shown opportunities for dose reduction using newer technologies and optimized protocols. This is the first report to describe variations in worldwide utilization of MPS hardware, software, and imaging protocols and their impact on radiation dose.

Methods: Data were submitted voluntarily to the International Atomic Energy Agency Nuclear Cardiology Protocols Study (INCAPS) registry, a multinational, cross-sectional study comprising 7911 imaging studies from 308 labs in 65 countries. We compared regional utilization of camera technologies, advanced post-processing software and protocol characteristics and analyzed the influence of each factor on effective dose (ED).

Results: Cadmium-zinc-telluride (CZT) and PET cameras were used in 10% (regional range 0-26%) and 6% (regional range 0-17%) of studies worldwide. Attenuation correction was used in 26% of cases (range 10-57%), and advanced post-processing software was used in 38% of cases (range 26-64%). 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. Factors associated with lower ED and odds ratio for achieving radiation dose ≤9 mSv included use of CZT, PET, attenuation correction, 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. Significant variability with use of dose-optimizing technology and protocols was observed between regions.

Conclusion: 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.

KEY WORDS:

Myocardial perfusion scintigraphy, SPECT, radiation dose reduction, nuclear cardiology protocols, camera technology

CONDENSED ABSTRACT

Advancements in MPS technologies and protocols have enabled significant opportunities to reduce patient radiation exposure. Drawn from the worldwide INCAPS registry, this is the first report to describe variations in worldwide utilization of dose optimizing technologies and protocols. We found that that newer technology cameras, advanced software, and stress-only imaging were associated with lower radiation dose. However, worldwide adoption of these practices was generally low and varied significantly between world regions, signifying further possibilities to optimize patient dose reduction across the globe.

ABBREVIATIONS:

AC = attenuation correction; CZT = cadmium-zinc-telluride; ED = effective dose; IAEA = International Atomic Energy Agency; INCAPS = IAEA Nuclear Cardiology Protocols Study; MBq = megabecquerel; mCi = millicurie; MPS = Myocardial perfusion scintigraphy; PET = positron emission tomography; SPECT = single-photon emission computed tomography; Tc-99m = technetium-99m; Tl-201 = thallium-201

INTRODUCTION

Cardiovascular disease (CVD) remains a leading cause of worldwide morbidity and mortality, resulting in 17.5 million deaths per year, including 7.4 million from coronary artery disease (CAD).(1) Myocardial perfusion scintigraphy (MPS) is an effective, non-invasive 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 (NCRP), 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.(4-8) This is particularly concerning to cardiology patients who may require repeat imaging, potentially subjecting them to greater lifetime exposure.(9) 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.(10-16) However, a growing body of evidence suggests that individual laboratory adherence to best practices may be lagging.(17-19)

Dose optimizing strategies recommended by the American Society of Nuclear Cardiology (ASNC) and the Society of Nuclear Medicine and Molecular Imaging (SNMMI) 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 (IAEA) to coordinate a worldwide cross-sectional study of MPS practice, the IAEA Nuclear Cardiology Protocols Study (INCAPS). Previous INCAPS publications have analyzed variations in regional doses, diagnostic reference levels, and adherence to best practices(17,19-25), but have not evaluated specific technologies. In this study, we compare regional utilization of camera technologies, advanced post-processing software, and imaging protocols and their impact on patient radiation dose.

METHODS

The methods of INCAPS have been previously described.(26) 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 in March-April 2013. An expert committee identified eight 'best practices' relating to radiation exposure. We evaluated the INCAPS data for worldwide variability in camera hardware, software technology, and protocols as they these best practices. 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 one week period, including: age, weight, gender, radiopharmaceutical type and activity injected, camera hardware, patient positioning (e.g., use of prone imaging), type of attenuation correction scan (CT or nuclear) 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 re-contacted to clarify potential omissions, errors, or discrepancies. All sites responded and clarified any discrepancies.

Radiation Dose

Radiation dose was quantified as the estimated 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 upon the radiopharmaceutical used and its activity according to dosimetry from the International Commission on Radiological Protection (ICRP).(27) ED was calculated according to the method of Senthamizhchelvan et al.(28) for Rb-82 PET MPS. The median dose for each site was evaluated for compliance with a target median ED of $\leq$ 9 mSv, as recommended by professional society guidelines.(29)

Statistical Analysis

Continuous variables are summarized as mean with standard deviation or median with interquartile range (IQR), where appropriate and compared between groups by analysis of variance or Kruskal-Wallis, test respectively. Categorical variables are compared by chi-squared test. Evaluation for independent variables that were associated with ED as a dependent variable was performed by univariable and multivariable linear regression. Logistic regression was performed for independent variables associated with a binary outcome of ED $\leq$ 9 mSv. A two-tailed $p<0.05$ was considered significant for all statistical tests. All analyses were conducted with Stata/SE 13.1 (StataCorp, College Station, TX, USA).

RESULTS

7911 studies from 308 sites in 65 countries were included. The mean patient age was 64 years and 59% were male. 39% of all studies (97% PET and 35% SPECT) were $\leq$9 mSv, while just 6% of all studies (32% PET and 4% single-photon emission computed tomography [SPECT]) achieved a dose $\leq$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 utilization 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. Use of multi-head SPECT gamma cameras ($p<0.001$), use of CZT cameras ($p<0.001$) and use of PET imaging ($p<0.001$) were all associated with significant reduction in patient radiation exposure. Worldwide geographic variability of CZT camera and PET imaging utilization are illustrated in **Figure 1a and 1b,** respectively.

Reconstruction software

Use of attenuation correction and use of advanced post-processing software are summarized in **Table 1**. Attenuation correction was used in 41% of all facilities and 26% of all cases worldwide. The highest proportion of cases was observed in Oceania (57%), followed by Asia (31%), Europe (27%), North America (26%), Latin America (12%), and Africa (10%). Attenuation correction SPECT was associated with decreased radiation exposure (9.0 vs. 10.3 mSv, $p<0.001$). Advanced post-processing software was used in 38% of sites, which was not associated with differences in estimated radiation dose ($p=0.48$). **Figure 1c** illustrates geographic variability in the use of attenuation correction.

Imaging protocols

Table 2 summarizes the breakdown of regional imaging protocols. Significant variations in protocol utilization 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 utilized in 90% of North American cases and 73% of Oceanic cases compared to only 14% of European cases. Tc-99m-labelled radiotracers were used in more than 93% of SPECT studies from every region except Asia, where 20% of studies were Tl-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.** Stress or rest-only protocols (OR 17.1, 95% CI 14.6-20.1, $p<0.001$), CZT cameras (OR 9.5, 95% CI 7.9-11.4, $p<0.001$), and PET cameras (OR 115.5, 95% CI 65.5-203.8, $p<0.001$) were among the factors most strongly associated with a significantly lower radiation dose and similarly most strongly 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 included use of newer technology cameras, use of attenuation correction or other 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 to 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 and colleagues showed that laboratories utilizing CZT cameras in combination with dose-reduced protocols could potentially achieve a dose reduction of 50% compared to conventional Tc-99m dosing and up to 75% compared to dual-isotope protocols.(30) 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.(31) For example, the total recommended administered activity for a Tc-99m two-day stress/rest protocol with a conventional SPECT gamma camera is listed as 16-24 mCi, whereas the activity recommended for newer technology cameras is only 8-12mCi.(14) Our data also showed that protocols utilizing CZT cameras 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 to single-head gamma cameras (7.1 vs. 12.6 mSv, $p < 0.001$) and 33% compared to multi-head gamma cameras (7.1 vs. 10.6 mSv $p < 0.001$). Despite this, use of CZT cameras was low in all world regions (range 0-26%), likely owing in large part to the substantial upfront cost of this technology.

Utilization of PET imaging was also low at just 6% of studies worldwide (range 0-17%), which may also 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. 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 $^{13}N\text{-}NH_3$ or $^{15}O\text{-}H_2O$, further raising the total cost of ownership.(32,33) However, some studies have shown that the use of PET MPS might actually reduce downstream costs associated with cardiac revascularization. Merhige et al. reported that use of PET MPS in patients with intermediate risk of CAD reduced rates of cardiac catheterization by more than 50% at one year while reducing costs by up to 30% when compared to conventional SPECT MPS.(33) The availability of perfusion radiotracers that can be obtained as a unit dose without expensive on-site equipment, such as ^{18}F-flurpiridaz, could also help to reduce cost and make PET cameras a more economical choice for cardiology imaging laboratories around the world. Where available, the use of 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 attenuation correction and advanced post-processing software, though the effect size for both was small in our sample. Particularly for advanced software, we believe this could indicate that laboratories were more likely to use this technology to reduce image acquisition time rather than patient radiation exposure. Al Badarin and colleagues 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 to 6.0 mSv for stress-only studies that did not use advanced post-processing software.(34) Additional literature shows that very low dose stress-first protocols performed on sodium-iodide SPECT cameras with administered activity of just 5 mCi (approx. 1.4 mSv dose) can provide adequate image quality with the use of advanced post-processing software.(35) 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.(36) Thus, there remains significant potential worldwide to realize greater dose optimization with advanced post-processing software.

Where attenuation correction 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. 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.(37,38) 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.(38) 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 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 one 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, and use of stress-first imaging. Similar to previous studies, we found that protocols adhering to these practices were associated with lower ED and increased likelihood of achieving a patient radiation dose ≤ 9 mSv.(17)

These findings must be interpreted in the context of inherent study limitations. First, the INCAPS was an observational study in which data were collected from each facility during a single week. Thus, the extent to which these data represent the complete distribution of studies performed at an individual laboratory is unknown. However, this was likely offset by sampling data from multiple laboratories in each region. INCAPS is also one of the largest registries of MPS studies, and represents the first regional data available in several world regions. 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.(36,39)

We also recognize that since the INCAPS implementation, which was carried out in 2013, 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 IAEA 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.

In this study, we observed that newer technology cameras, advanced software, and stress-only protocols were associated with reduced ED. Nevertheless, regional utilization 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.

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, utilization 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.

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FIGURE LEGENDS

Central Illustration: Worldwide and regional utilization of dose-optimizing technologies and protocols

- 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 stress-only protocols, CZT cameras, multiple positions, and PET cameras were less common.
- CZT = cadmium-zinc-telluride; PET = positron emission tomography

Figure 1: Geographic variability of technology and protocol utilization around the world

- World maps demonstrating the percentage of studies in each country utilizing (a) CZT cameras, (b) 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.
- CZT = cadmium-zinc-telluride; PET = positron emission tomography

Figure 2: Factors associated with achieving a dose of ≤ 9 mSv for MPS studies

- Odds ratios for performing ≤ 9 mSv MPS study were calculated using a multivariable logistic regression model. Note the logarithmic scale of the x-axis.

The largest effect size was seen with use of stress or rest-only protocols, CZT cameras, and PET cameras.

- CZT = cadmium-zinc-telluride; mSv = millisievert; PET = positron emission tomography;

Table 1. Comparison of regional laboratory camera technology, software, and imaging techniques.

Studies, n (%)	**Africa** 348	**Asia** 1469	**Europe** 2381	**Latin America** 1139	**North America** 2135	**Oceania** 439	**Total** 7911	**Mean ED** (mSv)	**Std dev** (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%)	1159 (79%)	1943 (82%)	1032 (91%)	1583 (74%)	322 (73%)	6336 (80%)	10.6	4.2
CZT	-	194 (13%)	312 (13%)	-	164 (8%)	113 (26%)	783 (10%)	7.1	3.2
PET	6 (2%)	50 (3%)	52 (2%)	-	362 (17%)	-	470 (6%)	3.7	2.4
Patient position									
Single position	267 (77%)	1415 (96%)	2195 (92%)	1090 (96%)	1996 (93%)	370 (84%)	7333 (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%)	1007 (69%)	1743 (73%)	1000 (88%)	1574 (74%)	190 (43%)	5826 (74%)	10.3	4.4
With AC	36 (10%)	462 (31%)	638 (27%)	139 (12%)	561 (26%)	249 (57%)	2085 (26%)	9	4.6
Software									
Standard	161 (46%)	877 (60%)	1347 (57%)	781 (69%)	1580 (74%)	159 (36%)	4905 (62%)	10	4.7
Advanced	187 (54%)	592 (40%)	1034 (43%)	358 (31%)	555 (26%)	280 (64%)	3006 (38%)	9.9	4.1

AC = attenuation correction; CZT = cadmium-zinc-telluride; ED = effective dose; mSv = millisievert; PET = positron emission tomography; Std dev = standard deviation.

Table 2. Distribution of regional study protocols and effective doses.

Protocol	Africa	Asia	Europe	Latin America	North America	Oceania	Total	Mean ED (mSv)	Std dev (mSv)	Median ED (mSv)	IQR (mSv)
1-day SPECT	**175**	**1121**	**1455**	**654**	**1661**	**402**	**5468**	**10.0**	**4.4**	**10.9**	**5.6**
Tc-99m											
Stress-only	109	122	421	53	52	40	797	3.9	1.7	3.4	2.4
Rest-only	6	43	133	81	12	3	278	5.0	1.7	4.9	2.5
Stress / rest	48	373	776	199	22	43	1461	9.7	2.9	9.6	3.6
Rest / stress	10	293	59	296	1549	284	2491	11.4	2.7	11.6	2.9
Dual isotope	-	105	6	11	24	-	146	21.2	3.0	21.6	2.9
Tl-201, 1 injection	-	166	39	1	2	17	225	14.5	2.6	15.5	3.9
Tl-201, 2 injections	-	19	21	13	-	5	58	18.4	3.4	19.2	3.9
Other 1-day SPECT	2	-	-	-	-	10	12	13.7	3.0	13.6	4.4
Multi-day SPECT	**167**	**295**	**874**	**485**	**111**	**37**	**1969**	**11.4**	**3.9**	**11.3**	**5.3**
Tc-99m stress / rest	145	238	599	166	57	2	1207	11.6	3.7	11.2	5.1
Tc-99m rest / stress	22	49	271	317	52	35	746	11.0	3.8	9.9	5.5
Other multi-day SPECT	-	8	4	2	2	-	16	19.1	8.4	20.7	6.5
PET	**6**	**53**	**52**	**-**	**363**	**-**	**474**	**3.7**	**2.5**	**3.6**	**1.5**
FDG viability study	6	17	9	-	11	-	43	9.2	5.2	7.5	6.7
Rb-82 rest / stress	-	11	30	-	339	-	380	3.3	0.8	3.5	1.2
N-13 NH3 rest / stress	-	19	7	-	10	-	36	2.8	1.2	2.9	1.6
Other PET	-	6	6	-	3	-	15	1.5	0.5	1.2	1.1
Total	**348**	**1469**	**2381**	**1139**	**2135**	**439**	**7911**	**10.0**	**4.5**		

ED = effective dose; FDG = fluorodeoxyglucose; IQR = interquartile range; mSv = millisievert; N = nitrogen; NH3 = ammonia; PET = positron emission tomography; Rb = rubidium; SPECT = single-photon emission computed tomography; Std dev = standard deviation; Tc = technetium; Tl = thallium.

Table 3. Factors with statistically significant correlation to ED based on a multivariable linear regression analysis.

Variables Associated with ED (mSv)	Beta	Standard Error	95% CI		P-value
			Lower	Upper	
Stress-only	-6.85	0.11	-7.06	-6.64	<0.001
Rest-only	-6.02	0.17	-6.35	-5.68	<0.001
Thallium scan	4.55	0.17	4.22	4.89	<0.001
Dual isotope	10.19	0.23	9.73	10.65	<0.001
2-day SPECT	0.16	0.08	0.00	0.31	0.044
CZT camera	-3.52	0.11	-3.73	-3.31	<0.001
Multi-head camera	-1.27	0.16	-1.59	-0.96	<0.001
Multiple positions	0.30	0.12	0.06	0.54	0.015
Attenuation correction	-0.56	0.08	-0.72	-0.40	<0.001
Advanced software	-0.54	0.07	-0.68	-0.40	<0.001
Lab volume	-0.01	0.00	-0.01	0.00	<0.001

CI = confidence interval; ED = effective dose; IQR = interquartile range; mSv = millisievert; SPECT = single-photon emission computed tomography.

Appendix

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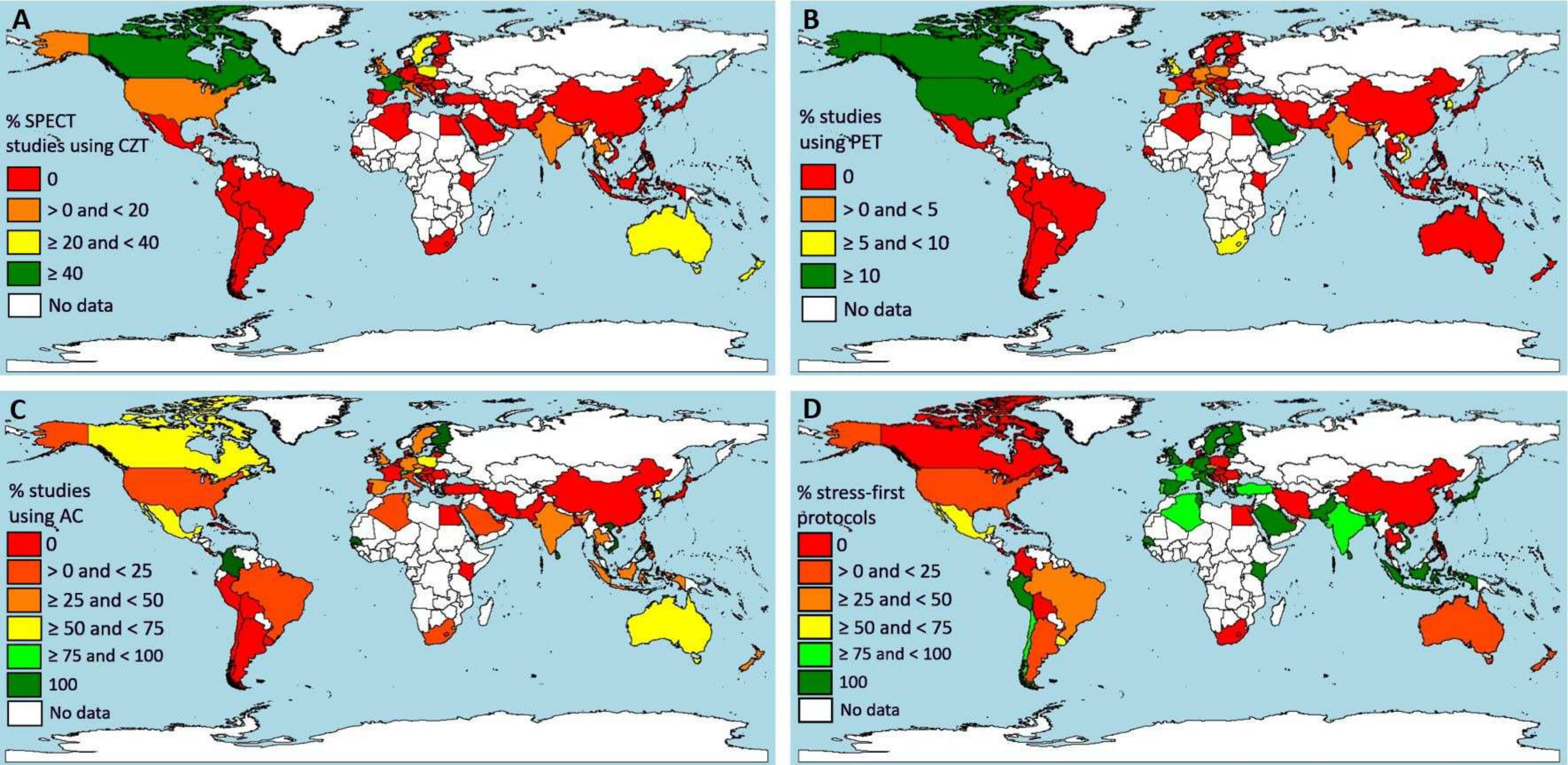
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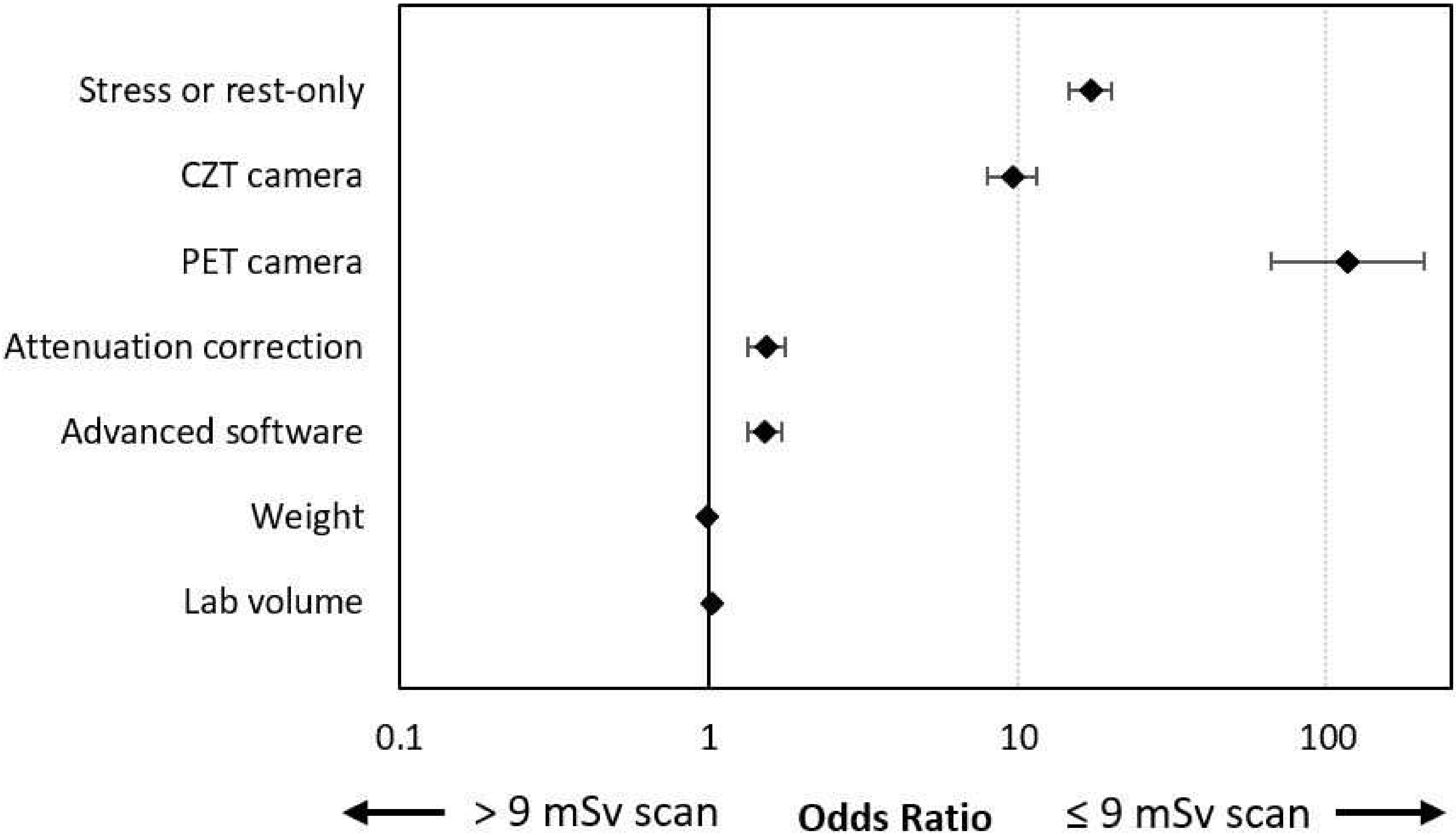

Stress or rest-only
CZT camera
PET camera
Attenuation correction
Advanced software
Weight
Lab volume
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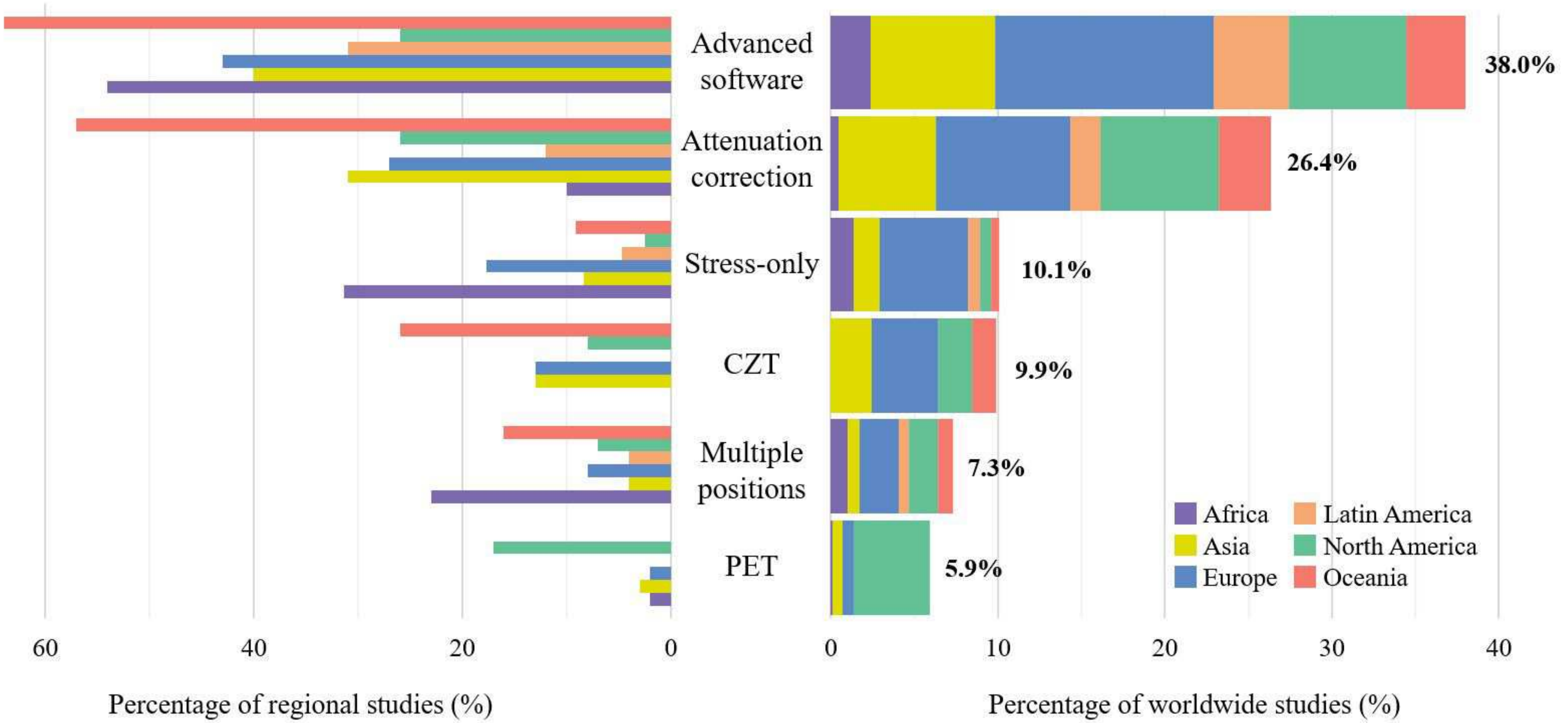
1
10
100
> 9 mSv scan
Odds Ratio
≤ 9 mSv scan


Advanced software
Attenuation correction
Stress-only
CZT
Multiple positions
PET
38.0%
26.4%
10.1%
9.9%
7.3%
5.9%
Africa
Asia
Europe
Latin America
North America
Oceania
60
40
20
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Percentage of regional studies (%)
Percentage of worldwide studies (%)