



Drivers of radiation dose reduction with myocardial perfusion imaging: A large health system experience

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Background. Despite increasing emphasis on reducing radiation exposure from myocardial perfusion imaging (MPI), the use of radiation-sparing practices (RSP) at nuclear laboratories remains limited. Defining real-world impact of RSPs on effective radiation dose (E) can potentially further motivate their adoption.

Methods. MPI studies performed between 1/2010 and 12/2016 within a single health system were included. Mean E was compared between sites with 'basic' RSP (defined as elimination of thallium-based protocols and use of stress-only (SO) imaging on conventional single photon-emission computed tomography (SPECT) cameras) and those with 'advanced' capabilities (sites that additionally used solid-state detector (SSD) SPECT cameras, advanced post-processing software (APPS) or positron emission tomography (PET) imaging), after matching patients by age, gender, and weight. Contributions of individual RSP to E reduction were determined using multiple linear regression after adjusting for factors affecting tracer dose.

Results. Among 55,930 MPI studies performed, the use of advanced RSP was associated with significantly lower mean E compared to basic RSP (7 ± 5.6 mSv and 16 ± 5.4 mSv, respectively; $P < 0.001$), with a greater likelihood of achieving $E < 9$ mSv (65.7% vs. 10.8%, respectively; OR 15.8 [95% CI 14 to 17.8]; $P < 0.0001$). Main driver of E reduction was SO-SSD SPECT (mean reduction = 11.5 mSv), followed by use of SO-SPECT + APPS (mean reduction = 10.1 mSv), ;ET (mean reduction = 9.7 mSv); and elimination of thallium protocols (mean reduction = 9.1 mSv); $P < 0.0001$ for all comparisons.

Conclusion. In a natural experiment with implementation of radiation-saving practices at a large health system, stress-only protocols used in conjunction with modern SPECT technologies, the use of PET and elimination of thallium-based protocols were associated with greatest reductions in radiation dose. Availability of several approaches to dose reduction within a health system can facilitate achievement of targeted radiation benchmarks in a greater number of performed studies. (J Nucl Cardiol 2020;27:785–94.)

Key Words: Myocardial perfusion imaging • radiation exposure • effective dose

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Abbreviations

CAD	Coronary artery disease
<i>E</i>	Effective dose
MPI	Myocardial perfusion imaging
PET	Positron emission tomography
RSP	Radiation-sparing practices
SO	Stress-only
SPECT	Single photon emission computed tomography
SSD	Solid-state detector

See related editorial, pp. 795–797

INTRODUCTION

Minimizing radiation exposure to patients undergoing radionuclide perfusion imaging has garnered increasing attention in recent years, driven by concerns about the potential long-term hazards of ionizing radiation and the desire to improve patient safety.^{1–3} As a result, major medical societies have issued recommendations for greater adoption of radiation-sparing interventions with myocardial perfusion imaging (MPI), in accordance with the central principles of radiation safety.^{4–6}

Several radiation-sparing practices (RSPs) are currently available for use with single photon emission computed tomography (SPECT) MPI.⁷ These range from simply avoiding radiopharmaceuticals with higher radioactivity, such as thallium-labeled tracers, to incorporating innovative hardware and software technologies and adoption of patient-centered imaging protocols aimed at lowering administered tracer dosage, and hence lowering radiation dose.^{8–11} The use of positron emission tomography (PET) offers another opportunity to assess myocardial perfusion with significantly lower radiation as compared with conventional SPECT.¹²

Radiation exposure from MPI at the majority of nuclear laboratories across the world, however, continues to exceed recommended targets.^{13–16} Furthermore, a smaller proportion of US-based laboratories achieve the endorsed levels of radiation exposure compared with non-US centers,¹⁷ with much of this variation in laboratory-level effective radiation dose (*E*) likely driven by slow and erratic adoption of RSPs within health systems in the US. This apparent disconnect between strong societal recommendations and suboptimal real-world RSP implementation may be partly due to limited evidence comparing the efficacy of different radiation-saving interventions, especially when implemented concurrently within the same laboratory.

To further clarify the advantages of RSP adoption, as has been achieved by several groups,^{18,19} it is critical to quantify radiation reductions with individual RSPs, in

order to better illuminate the potential for improvement in MPI safety. While the intention of the current study was not to describe novel approaches to dose reduction, we sought to determine the feasibility and outcomes of sequential RSP implementation within a single health system and to determine the contribution of each of these interventions to improvement in radiation exposure with MPI.

METHODS**Data Source and Participating Sites**

We used the electronic database of Saint Luke's Mid America Heart Institute to identify patients referred for clinically indicated SPECT or PET MPI studies between 1/1/2010 and 12/31/2016. The database includes information on MPI studies performed at multiple sites throughout the health system, including four large, hospital-based laboratories located within the Kansas City metropolitan area, and five affiliated, community-based sites located in surrounding rural communities. All studies are electronically transmitted, irrespective of the site of performance, to a central nuclear cardiology laboratory at the Saint Luke's Mid America Heart Institute (Kansas City, MO), where image processing takes place and information on patient demographics, risk factors, stress protocols, radiopharmaceutical used (type and administered activity), imaging protocol, and camera system use are entered by trained staff. Exercise or pharmacologic stress (with dipyridamole, adenosine, regadenoson, and dobutamine) was used according to standard protocols, and image acquisitions were completed in accordance with published guidelines.^{5,20} The study was reviewed and approved by the Institutional Review Board, and waiver for informed consent was granted based on the retrospective design of the study.

Definition of RSP Levels

The following practices were considered RSPs: elimination of thallium (Tl)-based protocols (including studies performed with Tl alone and dual-isotope studies), use of solid-state detector (SSD) cameras, use of stress-only (SO) protocols, utilization of advanced post-processing software (+APPS) with conventional SPECT cameras and use of PET.

Imaging sites within the network were grouped according to the level of RSP implementation. Sites with 'basic RSP' included those that implemented changes in radiotracer usage (namely elimination of Tl-based protocols) or adopted SO protocols on conventional SPECT cameras without adjunctive use of APPS. We chose this definition since such interventions can be adopted by any site performing cardiac radionuclide imaging without the need for major updates to existing imaging systems and are therefore reflective of what could be considered the most basic interventions to reduce *E* in "real-world" practices. Sites with 'advanced RSP', on the other hand, included those that additionally implemented hardware-

or software-based interventions, such as incorporation of SSD cameras, PET scanners or installation of APPS onto standard Anger cameras. Using these definitions, community-based, non-Metro imaging sites within the system ($n = 5$) were deemed to have ‘basic RSP’ capabilities while hospital-based sites ($n = 4$) were considered to have ‘advanced RSP’ capabilities. Sites with basic RSP were used as a comparator group in this analysis to provide a frame of reference for the changes in radiation exposure seen at sites with advanced capabilities. Notably, radiation reduction capabilities were comparable across sites within each group (Supplementary Table S1). Imaging equipment and processing software integration at participating sites are described below and summarized in Figure 1.

Selection and dosing of radiopharmaceuticals. During the study period, a combination of ^{99m}Tc -based, ^{201}Tl -based, or dual-isotope imaging protocols were used at sites with basic and advanced capabilities. However, the use of Tl-based SPECT imaging has gradually phased out, and these studies were no longer performed after the fourth quarter of 2012 at the main sites and after the third quarter of 2012 at outlying sites. The use of weight-adjusted radioisotope dose with SPECT was introduced at all sites early during the study period.

Camera systems and processing software. At the 4 metro locations, SPECT imaging was performed using a variety of conventional Anger SPECT cameras from a variety of vintages, with line source for attenuation correction, including two small field-of-view (CardioMD, Philips Healthcare, Milpitas, CA) and two large field-of-view cameras (ADAC, Philips Healthcare, Milpitas, CA). In the first quarter of 2010, an SSD SPECT camera (D-SPECT, Spectrum Dynamics, Sarasota, FL) was introduced at one of the main nuclear laboratories, and subsequently at one other major site in the third quarter of 2012. The use of SSD cameras enables the use of significantly lower radiotracer doses without compromising image quality, and these cameras were generally utilized in protocols to maximize radiation sparing rather than to shorten acquisition time. Participating non-metro sites used conventional large-field-of-view Anger SPECT cameras (Symbia Intevo, Siemens, Munich, Germany; ECAM, Siemens, Munich, Germany) with or without attenuation correction. These sites did not have access to SSD

camera technology or implementation of the APPS on their conventional camera systems.

Consistent implementation of APPS started in the 2nd quarter of 2012 with use of ASTONISH-128 (Philips Healthcare, Milpitas, CA); a processing software that involves iterative reconstruction and depth-dependent resolution recovery, in conjunction with an existing conventional small field-of-view SPECT camera (CardioMD, Philips Healthcare, Milpitas, CA). APPS implementation contributes to dose reduction either through allowing the use of lower tracer dosage in conjunction with full time imaging, or through enhancing image quality via the software specifications when used with full-dose tracer injection and shortened imaging duration.²¹

Imaging protocols. The use of SO protocols in appropriately selected patients was introduced at the four main imaging sites prior to the beginning of the study period.²² Imaging was performed with conventional SPECT systems (large field-of-view with line source attenuation correction), using low-dose (10-19.9 mCi) or high-dose (≥ 20 mCi) ^{99m}Tc injections. The availability of SSD cameras allowed the concomitant use of SO protocols on these camera systems, thereby enabling the use of ultra-low doses of ^{99m}Tc (less than 10 mCi), which was incorporated into the routine workflow of sites with SSD SPECT cameras. In addition, when APPS became available with small field-of-view Anger cameras at the main laboratories (the 2nd quarter of 2012), default protocols on those cameras were changed from high-dose stress-first to low-dose stress-first protocols (or ultra-low dose) became a routine practice at these sites.

Imaging protocols at the outlying imaging facilities, on the other hand, were limited to rest/stress or, occasionally high-dose SO protocols on conventional SPECT cameras (large field-of-view with or without attenuation correction).

Utilization of PET. PET MPI was consistently offered at the 4 main sites throughout the study duration. It was initially offered using a combination of PET/CT cameras and dedicated cardiac PET systems with line source attenuation correction. Furthermore, image acquisition was performed in both 2-D and 3-D modes. Later, all PET imaging took place on a variety of later generation PET/CT systems in 3-D mode. PET capabilities were not available at any of the outlying sites throughout the study duration.

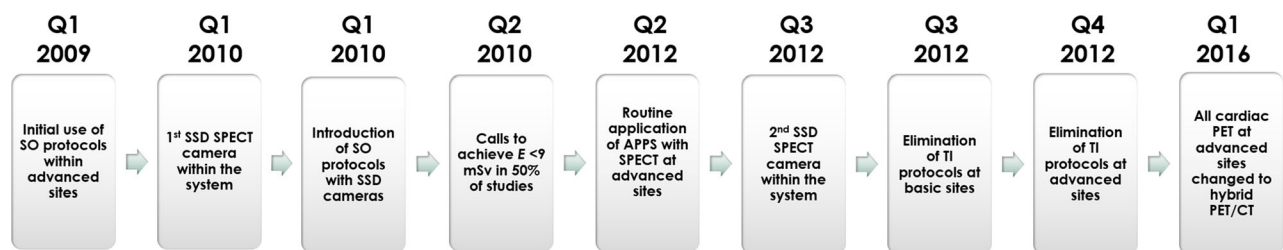


Figure 1. Timeline for the introduction of different radiation-sparing practices at participating sites.

Radiation-Dose Estimation

The administered dose of radiotracer (in mCi) for rest and stress acquisitions was recorded at the time of study performance and prospectively entered into the database. E was estimated from the administered radiotracer dose of ^{201}Tl and $^{99\text{m}}\text{Tc}$ -sestamibi using published conversion factors,^{23,24} and similarly for ^{82}Rb and ^{18}F -FDG.²⁵ $^{99\text{m}}\text{Tc}$ -tetrofosmin, which is associated with a lower radiation dose, was used in < 1% of the studies during the study period. Therefore, the same conversion formula for $^{99\text{m}}\text{Tc}$ -sestamibi was used to estimate E for these studies. Studies with missing data and those performed for purposes other than assessment of ischemia or viability using other radiopharmaceuticals (such as assessment of cardiac sympathetic nerve activity or assessment of possible cardiac amyloidosis) were excluded from the calculation of effective dose.

Contributions to E from ^{153}Gd line source transmission (for attenuation correction with SPECT MPI, estimated at 0.05 mSv), ^{68}Ge transmission (for attenuation correction with PET MPI, estimated at 0.08 mSv), or from low-dose CT (for attenuation correction on PET/CT camera systems, estimated at 0.5 mSv) were not included in final E estimates given the small magnitude of radiation contributed as compared with that associated with radiotracer injection.^{2,7}

Statistical Analyses

Demographics of patients who underwent MPI at sites with basic or advanced RSP capabilities were compared using t -tests for continuous variables and χ^2 for categorical variables. Mean achieved E was compared between sites with basic and advanced RSP, in the overall population and in an age-, gender- and weight-matched (5:1) population, using paired sample t test. Matching was performed to account for differences in patient characteristics that may affect radiation dose. The adequacy of the match was verified by reporting P values between the distributions. The proportion of studies performed with $E < 9$ mSv in each group was also compared using χ^2 test.

Afterward, absolute reduction in E achieved with individual radiation saving interventions was determined, using R/S conventional SPECT without implementation of any additional RSP as a reference. This was accomplished using multiple linear regression after adjusting for covariates potentially affecting radiation dose (weight) or test selection (age, gender, presence of CAD, prior revascularization, prior stroke, peripheral arterial disease, left bundle branch block and chronic obstructive pulmonary disease), and with E as the outcome variable. For the purpose of the last aim, studies performed at sites with advanced and basic capabilities were analyzed separately. All analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, NC, USA).

RESULTS

Comparison of Effective Doses by RSP Level

During the study period, a total of 55,930 MPI studies were performed; of them 52,735 (94.3%) were performed at sites with advanced RSP and the rest at sites with basic capabilities. There were differences in patient characteristics between sites, such that patients who underwent MPI at advanced RSP sites were older and more often males with lower BMI compared to those who underwent testing at sites with basic capabilities. Therefore, patients were matched (5:1) by age, gender, BMI and year of testing. The matched cohort comprised 17,976 patients, of whom 14,980 imaged at sites with advanced RSP and 2996 patients at sites with basic RSP. The mean age of the matched cohort was 63.8 ± 12.1 years and BMI of 33.1 ± 7.4 with predominance of female patients (53.2%). Characteristics of patients by imaging sites before and after matching are shown in Table 1.

Mean E was lower at sites with advanced capabilities compared to those having only basic capabilities

Table 1. Comparison of patient characteristics and effective doses between sites with and without advanced RSP capabilities, before and after matching for patient characteristics

	Before match			After 5:1 match		
	Advanced RSP	Basic RSP	<i>P</i> -value	Advanced RSP	Basic RSP	<i>P</i> -value
N	52735	3195		14980	2996	
Age (years)	65.5 ± 12.2	62.9 ± 12.9	< .001	63.8 ± 12.1	63.8 ± 12.2	.94
Women (%)	23333 (44.2)	1741 (54.5)	< .001	7970 (53.2)	1594 (53.2)	1.0
BMI (kg/m ²)	30.5 ± 7.2	33.7 ± 9.1	< .001	33 ± 7.3	33.1 ± 7.4	.58
E (mSv)	6.3 ± 7.6	17.7 ± 9.5	< .001	7 ± 5.6	16 ± 5.4	< .001
$E < 9$ mSv (%)	37107 (70.4)	334 (10.5)	< .001	9840 (65.7)	325 (10.8)	< .001

Continuous variables presented as mean ± standard deviation; categorical variables as percentages
BMI, body mass index; E , effective dose; RSP, radiation-sparing practices; SD, standard deviation

(6.3 ± 7.6 vs. 17.7 ± 9.5 mSv, mean between-group difference of 10.8 ± 8.2 mSv, $P < 0.001$). This difference persisted after matching for patient characteristics (7 ± 5.6 vs. 16 ± 5.4 mSv, mean between-group difference of 9.5 ± 11.2 mSv, $P < 0.001$). In addition, a greater proportion of studies performed at sites with advanced capabilities was done with an effective dose < 9 mSv per study compared to those done at sites with only basic RSP capabilities: 70.4% and 8.9%, respectively, in the unmatched cohort (OR of 24.5; [95% CI 22.1 to 271]; $P < 0.001$) and 65.7% vs. 10.8%, respectively, in the matched cohort (OR 15.8; [95% CI 14 to 17.8]; $P < 0.001$).

Reduction in Effective Dose with Individual RSPs

Mean E and patient-dependent determinants of testing modality were then compared across the RSP spectrum within sites with advanced RSP capabilities (Table 2). Mean E was significantly different between various RSPs; TI-based protocols were associated with the highest mean E (22.3 ± 8.7 mSv) whereas SO-SSD SPECT was associated with the lowest mean E (1.9 ± 1.8 mSv, P value for between-group comparison < 0.001). In addition, there were significant differences in age, gender, BMI and prevalence of CAD, prior revascularization, prior stroke, peripheral arterial disease, left bundle branch block, and chronic obstructive pulmonary disease across the groups (P value for all between-modality comparisons < 0.001). In addition, dose of radiopharmaceutical varied significantly between interventions, with the highest total ^{99m}Tc dose used for patients who underwent R/S SPECT without RSP (48.7 ± 13.8 mSv in advanced RSP sites and 57.8 ± 12.1 mSv in basic RSP sites) and the lowest in patients who underwent SO-SSD SPECT (6.5 ± 6.2 mSv), followed by SO-SPECT + APPS (9.3 ± 0.7 mSv), both only available at advanced sites (Supplementary Table S2).

In a model adjusted for the covariates above, mean reduction in E relative to R/S SPECT without use of RSP, was greatest with SO-SPECT on SSD camera (mean reduction of 11.5 mSv, 95% CI [11.3 to 11.7], $P < 0.001$), followed by SO-SPECT on conventional camera with APPS (mean reduction = 10.1 mSv, 95% CI [9.8 to 10.4], $P < 0.001$); PET MPI (mean reduction = 9.7 mSv, 95% CI [9.6 to 9.9], $P < 0.001$); elimination of TI-based protocols (mean reduction = 9.1 mSv, 95% CI [8.5 to 9.7], $P < 0.001$); R/S SPECT on SSD camera (mean reduction = 6.4, 95% CI [6.2 to 6.7], $P < 0.001$); SO-SPECT with conventional cameras (mean reduction = 6 mSv, 95% CI [5.7 to 6.2], $P < 0.001$), and least with R/S SPECT + APPS (mean

reduction = 1.9 mSv, 95% CI [1.6 to 2.1], $P < 0.001$) (Figure 2).

DISCUSSION

In this study, we examined the association between the implementation of RSPs and radiation exposure at a group of nuclear laboratories within a single health system. Our data show that a significantly lower E can be achieved at sites incorporating advanced RSP options into workflow, relative to other sites where RSP implementation was more basic. Furthermore, the current detailed comparison among RSPs provides knowledge about the relative efficacy of various dose-reducing strategies. Use of SO protocols in conjunction with innovative SPECT technologies (including SSD cameras or APPS) resulted in the most marked reductions in E , followed by PET MPI and avoidance of TI-based protocols, whereas use of SO protocol with conventional cameras without APPS, or use of R/S protocol with SSD cameras were associated with more modest, but still significant, degrees of E reduction.

In the current era, nuclear laboratories face the challenge of accommodating patients with varying degrees of complexity and cardiovascular risk, and hence there has been growing emphasis on providing a patient-centered approach to imaging.²⁶ As a result, a nuclear laboratory of the modern time needs to be equipped with a wide range of imaging capabilities that can be tailored to meet patients' needs. Our data provide a frame of reference for physicians ordering MPI to help inform selection of a modality that offers an optimal risk/benefit balance for any given patient. Furthermore, determining the relative efficacy of different RSP's helps guide laboratories exploring the addition of RSP into their workflow. The current findings should be considered in the context of a guide approximating expected improvements in radiation exposure if a given RSP is implemented—after establishing technical, financial, and logistical feasibility of incorporating that intervention—rather than an endorsement of one intervention over others.

This study also demonstrates that SO protocols can have variable impact on radiation dose, depending on the camera system used (Figure 3). For example, combining SO protocol with conventional small field-of-view SPECT cameras equipped with APPS or with SSD cameras allows the use of low or ultra-low ^{99m}Tc doses, and hence achieving the largest reduction in E . On the other hand, when SO is used in conjunction with conventional large field-of-view SPECT cameras without APPS, larger ^{99m}Tc doses are needed to achieve diagnostic-level studies, and the observed reduction in E would be therefore more modest. Understanding the

Table 2 continued

	Sites with advanced RSP TI-based SPECT	P-value	Sites with basic RSP No RSP (R/S SPECT)	SO-SPECT	TI-based SPECT	P-value
Stroke (%)	6 (4.6%)	< .0001	-	-	-	-

* *P* value for across-modality comparison within groups
 Continuous variables presented as mean ± standard deviation; categorical variables as percentages
APPS, advanced post-processing software; *BMI*, body mass index; *CAD*, coronary artery disease; *COPD*, chronic obstructive pulmonary disease; *E*, effective dose; *LBBB*, left bundle branch block; *PAD*, peripheral arterial disease; *R/S*, rest/stress; *SD*, standard deviation; *SO*, solid-state detector

strengths and limitations of each of the camera systems is critical when balancing the benefits of dose-reducing interventions with the potential risks of adversely affecting diagnostic quality of radionuclide perfusion imaging studies.

Reducing effective dose in association with RSP adoption also has significant public safety implications, considering the number of MPI studies performed annually.¹ Adopting a simple RSP such as eliminating thallium would translate into substantial population-level radiation savings and, in turn, possibly into a potentially significant number of prevented cancers,²⁷ underscoring the relevance of lowering radiation burden with MPI. Such benefits could be potentially amplified if multiple RSP's are used synergistically within a single testing site.

In a survey of nuclear laboratories worldwide, adherence to laboratory 'best practices', including some of the practices considered in the RSP definition used in our study, was associated with reduction in laboratory-level radiation dose.¹³ The current findings extend those by the INCAPS investigators by providing a more exhaustive evaluation of the efficacy of other radiation-saving interventions—including PET and use of SSD cameras—and by quantification of the benefits of RSP adoption on radiation exposure.

Study Limitations

The use of *E* as a marker of per-study radiation exposure, while it was originally described to assess population effective dose, may not be perfectly accurate, and this issue has been described before.² Secondly, this study reflects the experience of a single center committed to improving RSP adoption over time. It is conceivable that other sites with access to the same capabilities may have different utilization rates of individual RSP compared to our center. As a result, such sites may achieve a different overall reduction in *E*; however, efficacy of individual interventions should remain similar, provided patients' characteristics are similar to those included in the current study. Lastly, the current study design does not allow the examination of other recommended practices to reduce radiation dose, such as screening for the appropriateness of ordered studies or avoiding imaging altogether.

CONCLUSION

Adoption of advanced radiation-sparing practices is associated with marked reduction in MPI radiation burden, and implementation of such practices significantly increases the likelihood of achieving recommended radiation targets, whereas adoption of

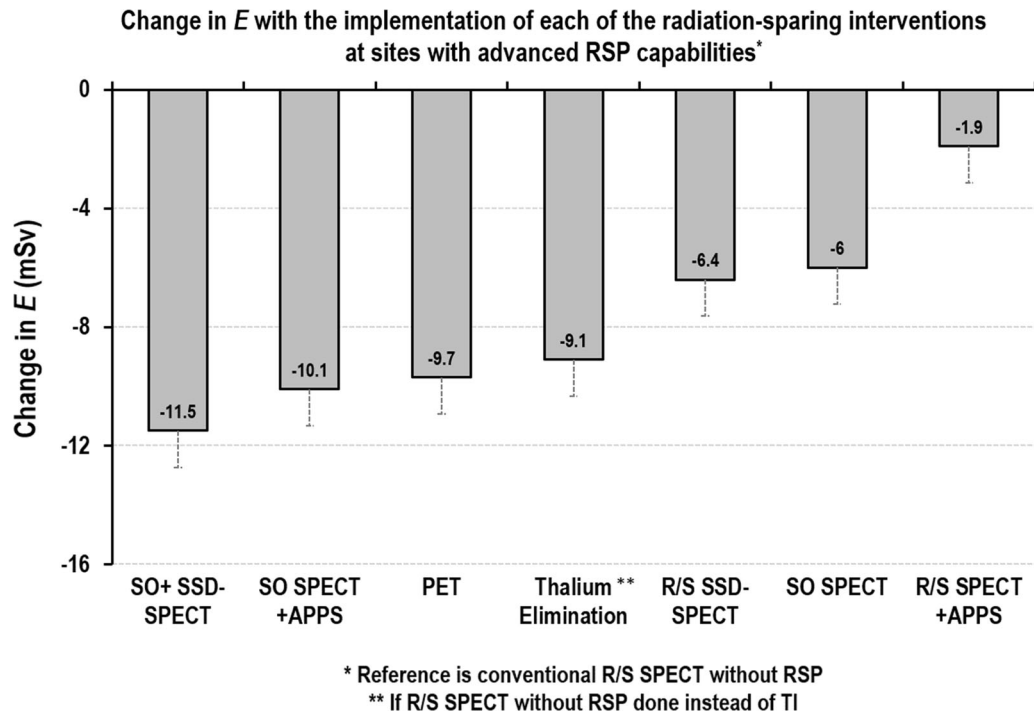


Figure 2. Change in E with the implementation of each radiation-sparing practice at sites with advanced RSP capabilities. Graph depicts change in E using each of the radiation-sparing interventions (adjusted for age, gender, BMI, and other factors that may influence selection of RSP modality), if that particular intervention is used instead of R/S conventional SPECT without RSP.

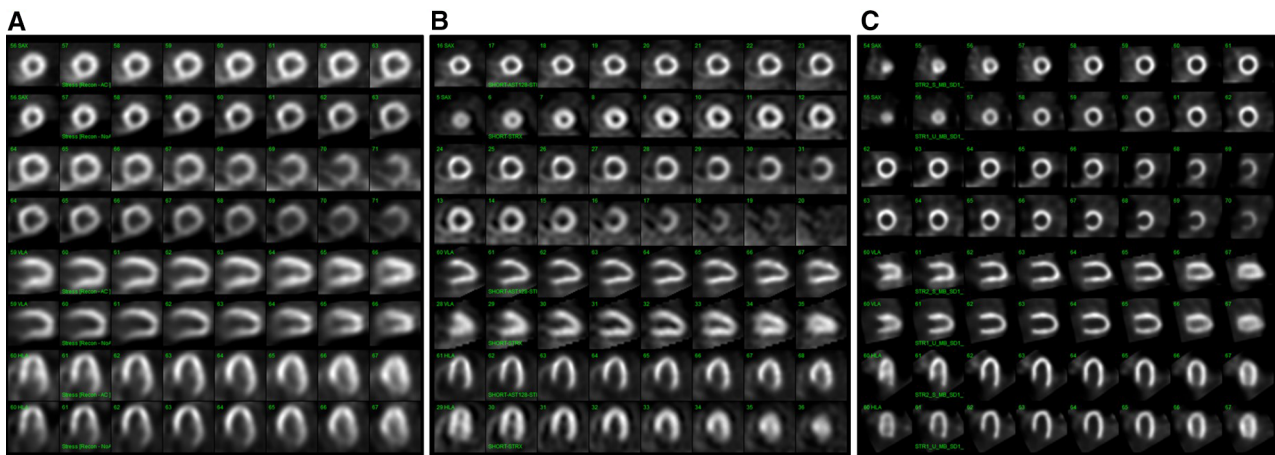


Figure 3. Examples of stress-only application with various SPECT imaging systems. This figure shows different applications of stress-only (SO) protocols with SPECT MPI and effective radiation dose associated with each of these studies. **A** a normal exercise SO-SPECT study performed on a large field-of-view Anger camera with (upper row) and without attenuation correction (lower row) after injection of 29.5 mCi of ^{99m}Tc (effective dose 8.7 mSv). In **B**, a normal exercise SO-SPECT performed on a small field-of-view Anger camera with image processing done using Astonish 128[®], an advanced post-processing software that involves iterative reconstruction and depth-dependent resolution recovery (upper row). The same study was also processed using traditional filtered back projection (lower row) with clear difference in the quality of the images. This patient was injected with 9.6 mCi of ^{99m}Tc (effective dose 2.8 mSv). **C** a normal exercise SO-SPECT performed on an SSD SPECT camera in the supine (upper row) and upright positions (lower row) after injection of 5.5 mCi (effective dose 1.6 mSv).

more basic radiation-saving interventions results in more modest radiation reduction. The efficacy of interventions across the radiation-sparing spectrum varied significantly, with use of stress-only protocols in conjunction with solid-state detector SPECT cameras or conventional SPECT cameras equipped with advanced post-processing software, use of PET MPI and elimination of thallium-based protocols being the practices associated with the greatest reductions in radiation effective dose. Realizing such differences among radiation-saving interventions can allow nuclear laboratories to design radiation-reduction strategies that help them meet radiation targets.

NEW KNOWLEDGE GAINED

The current data describe improvement in radiation dose following sequential implementation of radiation-saving practices within a large health system and demonstrate that the most effective interventions were use of stress-only protocols in conjunction with solid-state detector cameras or advanced post-processing-equipped conventional SPECT cameras, use of positron emission tomography and elimination of Tl-based protocols.

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