

Coronary Artery Calcification Screening

Estimated Radiation Dose and Cancer Risk

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Background: Multidetector computed tomography has been proposed as a tool for routine screening for coronary artery calcification in asymptomatic individuals. As proposed, such screening could involve tens of millions of individuals, but detailed estimates of radiation doses and potential risk of radiation-induced cancer are not currently available. We estimated organ-specific radiation doses and associated cancer risks from coronary artery calcification screening with multidetector computed tomography according to patient age, frequency of screening, and scan protocol.

Methods: Radiation doses delivered to adult patients were calculated from a range of available protocols using Monte Carlo radiation transport. Radiation risk models, derived using data from Japanese atomic bomb survivors and medically exposed cohorts, were used to estimate the excess lifetime risk of radiation-induced cancer.

Results: The radiation dose from a single coronary artery calcification computed tomographic scan varied more than 10-fold (effective dose range, 0.8-10.5 mSv) depending on the protocol. In general, higher radiation doses were associated with higher x-ray tube current, higher tube potential, spiral scanning with low pitch, and retrospective gating. The wide dose variation also resulted in wide variation in estimated radiation-induced cancer risk. Assuming screening every 5 years from the age of 45 to 75 years for men and 55 to 75 years for women, the estimated excess lifetime cancer risk using the median dose of 2.3 mSv was 42 cases per 100 000 men (range, 14-200 cases) and 62 cases per 100 000 women (range, 21-300 cases).

Conclusions: These radiation risk estimates can be compared with potential benefits from screening, when such estimates are available. Doses and therefore risks can be minimized by the use of optimized protocols.

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COMPUTED TOMOGRAPHY (CT) has been proposed as a tool for routine screening for coronary artery calcification (CAC) in asymptomatic individuals as part of a comprehensive risk assessment. A national survey in the United States reported that approximately 27% of diagnostic radiologists already read CAC CT

in the United States could involve tens of millions of individuals. However, the benefits from this type of screening have not yet been demonstrated directly in randomized trials with cardiovascular events or mortality as an end point, but it has been suggested that the use of CAC scoring can detect disease in asymptomatic persons who would be at low risk when assessed by traditional risk factors.³ However, the potential risks of screening, including the risk of radiation-induced cancer, have to be considered along with the potential benefits.

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It is impractical to estimate the risk of radiation-induced cancer from CT scans directly through an observational study, because such a study would require the follow-up of hundreds of thousands of patients for their entire lifetime.⁴ The difficulty was also underscored in a recent study.⁵ The magnitude of the risks can be

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screening scans regularly, making it the most common type of CT screening currently performed in the United States.¹ The Screening for Heart Attack Prevention and Education (SHAPE) guidelines recommend screening of all asymptomatic men 45 to 75 years of age and asymptomatic women 55 to 75 years of age except those defined as very low risk.² Such screening

Table 1. Computed Tomographic Scan Protocols for Coronary Artery Calcification Screening and Protocol Parameters

Protocol Source	Scanner	Scan Mode	ECG Synchronization	Tube Potential, kVp	Gantry Rotation Time, s	Tube Current-Time Product, mAs ^a	Detector Configuration, mm	Pitch ^b
Study 1 ^{22,23}	LightSpeed QX/i	Axial	Retrospective	120	0.8	320 (400)	4 × 2.5	1
	LightSpeed Plus	Axial	Prospective	120	0.5	104 (130)	4 × 2.5	1
	Volume Zoom	Axial	Prospective	140	0.5 or 0.361	50 (63)	4 × 2.5	1
Study 2 ^{20,21}	LightSpeed Pro 16	Axial	Prospective	120	0.5	104 (130)	4 × 2.5	1
	Sensation 16	Axial	Prospective	140	0.5	50 (63)	12 × 1.5	1
	Sensation 64	Axial	Prospective	120	0.33	50 (63)	30 × 0.6	1
	Aquilion 64	Axial	Prospective	135	0.33	48 (61)	4 × 3.0	1
Study 3 ¹⁹	LightSpeed 16	Axial	Prospective	120	0.5	106 (132)	8 × 2.5	1
	Sensation 16	Axial	Prospective	120	0.42 or 0.37	70 (88)	6 × 3.0	1
Study 4 ²⁴	LightSpeed Plus	Axial	Prospective	120	0.5	70 (25-145)	4 × 2.5	1
	MX 8000	Axial	Prospective	120	0.5	30 (10-65)	4 × 2.5	1
	Volume Zoom	Axial	Prospective	120	0.5	55 (20-135)	4 × 2.5	1
	Volume Zoom	Spiral	Retrospective	120	0.5	50 (20-115)	4 × 2.5	0.375
	Aquilion	Axial	Prospective	120	0.5	45 (20-90)	4 × 3.0	1
	Sensation 64	Spiral	Retrospective	120	0.33	70 (20-145)	64 × 0.6	0.2
Hospital 1 ^c	Precedence 16P	Axial	Prospective	120	0.5	70	8 × 3.0	1
	LightSpeed VCT	Axial	Prospective	120	0.35	70-88	8 × 2.5	1
Hospital 2 ^c	Brilliance 64	Axial	Prospective	120	0.4	50 (20-120)	40 × 0.625	1
	Definition	Axial	Prospective	120	0.33	95 (45-195)	6 × 3.0	1
Hospital 3 ^c	Definition	Axial	Prospective	120	0.33	150	6 × 3.0	1

Abbreviations: kVp, kilovolt peak; mAs, milliampere seconds.

^aSome protocols provide different mAs by patient size. Numbers in parentheses for studies 1, 2, and 3 protocols are mAs for patients who weighed more than 100 kg. Numbers in parentheses for study 4 and hospital 2 protocols are mAs for small and large patients. The hospital 1 protocol for the LightSpeed VCT scanner also provides a range of mAs for adjustment based on patient habitus.

^bPitch is applied to spiral scans. It indicates pitch for spiral scans defined as the ratio of the table feed per x-ray tube rotation to the x-ray beam width. For axial scans, it indicates ratio of the table increment between successive x-ray beam rotations to the x-ray beam width.

^cProtocols currently used clinically at 3 different university hospitals: hospitals 1 through 3 indicate Columbia University/New York–Presbyterian Hospital, New York, New York; Cleveland Clinic, Cleveland, Ohio; and Penn State University, Hershey, Pennsylvania, respectively.

estimated indirectly by extrapolating risk models from existing long-term studies of the effects of radiation exposure, such as the Life Span Study of Japanese atomic bomb survivors.⁶⁻⁸

In the present study, we reviewed a number of protocols for CAC screening by multidetector CT (MDCT) to estimate organ-specific radiation doses. We then used the radiation risk models from the National Research Council's Biological Effects of Ionizing Radiation (BEIR) VII committee to estimate the potential radiation-induced cancer risk from screening according to age and sex.

METHODS

CT PROTOCOLS

We reviewed the literature for recent protocols for CAC measurement using MDCT. Unlike other cardiac imaging modalities, such as nuclear medicine and echocardiography, where protocols are more standardized,^{9,10} cardiac CT protocols still vary widely depending on institutions and scanners. There have been no agreed-on standard scan protocols for CAC measurement by MDCT, and various protocols have been used in previous studies.¹¹⁻¹⁸ In the present study, we considered CT scan protocols that were established by some national cardiac studies¹⁹⁻²³ and by one international study on standardization in cardiac CT.²⁴ In practice, most CT technologists are not believed to adjust the calcium scoring protocols much. They use a default protocol by just adjusting scan area. Also, protocols currently used clinically at 3 different university hospitals (Columbia University/New York–Presbyterian Hospital, New York, NY; Cleveland Clinic, Cleveland, Ohio; and Penn State University, Hershey,

Pennsylvania) were included. The protocols, including technical parameters, are summarized in **Table 1**.

RADIATION DOSE CALCULATION

Radiation doses were calculated using the CT scan protocols and CT dosimetry programs (CTDosimetry version 0.99x and CT-Expo version 1.6).^{25,26} The programs use organ dose databases generated based on Monte Carlo radiation transport modeling by the National Radiological Protection Board in the United Kingdom and the National Research Center for Environment and Health in Germany.²⁷⁻³⁰

According to the CT operational manuals for studies 1 through 3, each participant receives 2 scans for the purposes of increased reliability and quality control.^{19-21,23} The double scan is performed for research purposes and is not typical clinical practice. Therefore, radiation dose calculation and risk estimation in this study was performed assuming only a single CT scan per participant. The studies and scanner-specific CT setting parameters presented in Table 1 were used for dose calculation, with the additional assumption that the typical scan length is 12 cm.¹⁷ Some protocols provide a range of x-ray tube current-time products (milliampere seconds [mAs]) for patients of different sizes. For these protocols, tube current-time products for medium-size patients were used for dose calculation. Organ-specific radiation doses and the effective dose for each protocol were calculated. The effective dose is the sum of weighted absorbed doses in all irradiated tissues and organs in the body and describes nonuniform dose in order of equivalent whole-body dose.³¹ The effective dose is one of the most frequently reported dosimetric quantities from CT scans. International Commission on Radiological Protection publication 103 tissue-weighting factors were used to calculate the effective dose.³²

Table 2. Organ-Specific and Effective Dose Estimates for Each Coronary Artery Calcification Computed Tomographic Screening Protocol

Scanner	Organ Dose, mGy						Effective Dose, mSv ^a
	Breasts	Lungs	Esophagus	Bone Marrow	Liver	Skin	
Study 1							
LightSpeed QX/i	36.0	28.0	16.0	5.6	5.3	4.1	10.5
LightSpeed Plus	12.0	9.4	5.4	1.9	1.7	1.4	3.5
Volume Zoom	8.1	5.4	2.9	1.1	1.0	0.9	2.2
Study 2							
LightSpeed Pro 16	11.0	8.9	5.1	1.8	1.7	1.3	3.3
Sensation 16	8.1	5.4	2.9	1.1	1.0	0.9	2.2
Sensation 64	3.8	3.1	1.8	0.6	0.6	0.4	1.1
Aquilion 64	8.5	6.5	3.8	1.3	1.2	1.0	2.5
Study 3							
LightSpeed 16	11.0	8.9	5.5	1.9	1.7	1.3	3.4
Sensation 16	5.8	4.4	2.6	0.9	0.9	0.6	1.7
Study 4							
LightSpeed Plus	7.9	6.2	3.5	1.2	1.2	0.9	2.3
MX 8000	2.6	2.0	1.2	0.4	0.4	0.3	0.8
Volume Zoom, axial	4.6	3.5	2.0	0.7	0.7	0.5	1.3
Volume Zoom, spiral	11.0	8.5	4.9	1.7	1.6	1.2	3.1
Aquilion	7.4	4.7	2.6	0.9	0.8	0.9	1.9
Sensation 64	27.0	22.0	13.0	4.5	4.2	3.1	8.0
Hospital 1							
Precedence 16P	5.7	4.4	2.5	0.9	0.8	0.6	1.7
LightSpeed VCT	7.7	6.4	3.9	1.2	1.2	0.9	2.3
Hospital 2							
Brilliance 64	4.1	3.1	1.8	0.6	0.6	0.5	1.2
Definition	9.0	5.5	1.2	0.9	2.1	1.0	2.3
Hospital 3							
Definition	14.1	8.6	1.8	1.4	3.3	1.5	3.6

^aEffective dose based on International Commission on Radiological Protection publication 103 tissue-weighting factors.³²

CANCER RISK ESTIMATION

We used the radiation risk models for sex- and organ-specific cancer incidence that were developed by the BEIR VII committee³³ combined with our organ-specific dose estimates to estimate the risk of radiation-induced cancer. Site-specific models were not available for some cancer sites, such as the esophagus, pancreas, skin, and kidney; therefore, cancer risks at these sites were estimated using the radiation coefficients from the excess relative risk model for “other solid cancers” in the BEIR VII report. For most cancer sites, the committee’s risk models were estimated using data from the Life Span Study of the Japanese atomic bomb survivors³³; the major exceptions were the risk models for breast cancer and thyroid cancer. The breast cancer model was based on an excess relative risk model from a pooled analysis of 8 cohort studies, including both atomic bomb survivors and medically exposed individuals, by Preston et al.³⁴ Thyroid cancer was based on a pooled analysis of 7 studies by Ron et al.³⁵ Background cancer incidence rates for the general US population were estimated using site-specific cancer incidence rates for all races from the Surveillance, Epidemiology and End Results Program cancer registries for 2000 through 2005.³⁶

After an initial lag period (assumed to be 5 years for solid cancers and 2 years for leukemia), the risk of radiation-induced cancer remains elevated for the rest of the person’s lifetime.³⁷ Therefore, the total risk of radiation-induced cancer was calculated using life table methods as a cumulative lifetime risk with adjustment for competing causes of death made using all-cause mortality rates for the US population.³⁸ Potential radiation-induced cancer risks from CAC screening by MDCT were estimated according to age at screening and sex. The SHAPE

guidelines recommend screening of all asymptomatic men 45 to 75 years of age and asymptomatic women 55 to 75 years of age except those defined as being at very low risk.² While SHAPE suggests screening with either CAC or carotid intima-media thickness measurement, the former is more reproducible and predictive of future events,³⁹ and it would be expected that most patients would therefore undergo CAC screening. There are approximately 50 million persons in the United States who are within the age range recommended for CAC screening by the SHAPE guidelines. The SHAPE guidelines recommended reassessment within 5 years for those with a positive test result for atherosclerosis and every 5 to 10 years for those with a negative test result. In the present study, we estimated cancer risks under 2 different scenarios. First, we estimated radiation-induced cancer risk from a single CAC screening by MDCT at any age between 40 and 80 years for each of the different protocols. Second, we estimated the total radiation-induced cancer risk in accordance with the SHAPE guidelines: repeated CT screening every 5 years from the age of 45 to 75 years for men and 55 to 75 years for women.

RESULTS

RADIATION DOSE

The estimated effective dose from a single CAC screening varied widely from 0.8 to 10.5 mSv across the CT protocols (**Table 2**). The median and mean values were 2.3 and 3.1 mSv, respectively. The organs or tissues that were estimated to receive measurable radiation doses, in ap-

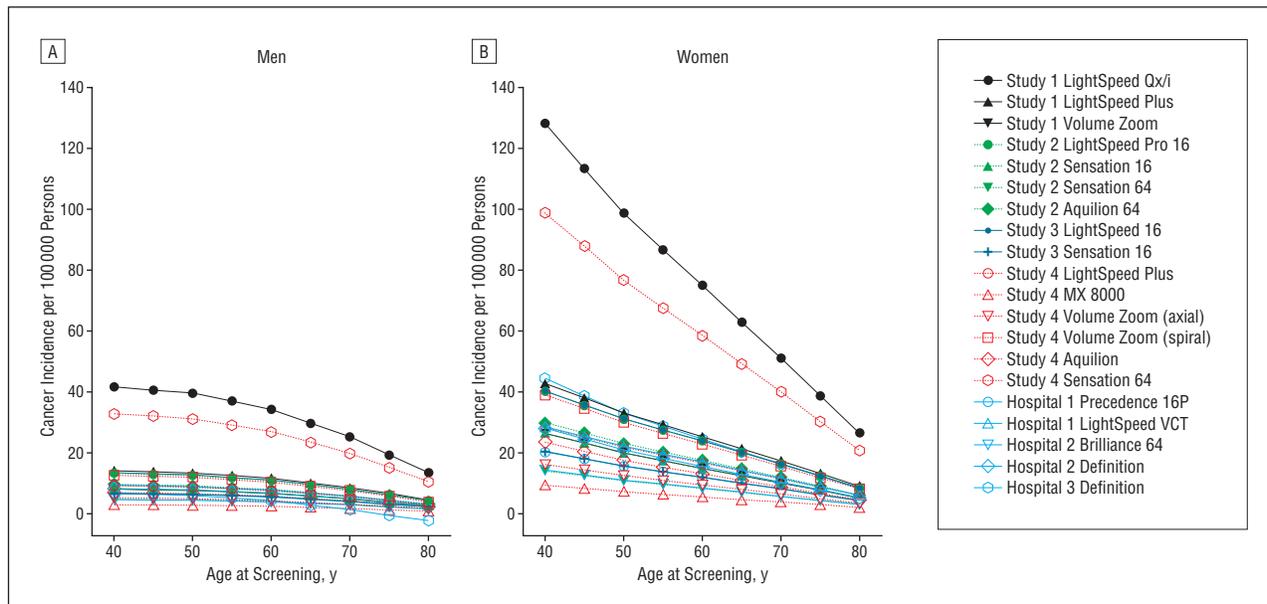


Figure. Estimated lifetime risk of radiation-induced cancer per 100 000 persons from a single computed tomographic scan to assess coronary artery calcification by age at screening.

proximate order of magnitude, were breast, lung, thymus, esophagus, bone surface, adrenal glands, bone marrow, liver, pancreas, skin, spleen, muscle, stomach, and kidney. The wide variation in radiation doses can be attributed to many factors, including different CT scanner models and different CT scan techniques. In general, higher radiation doses were associated with higher x-ray tube current, higher tube potential, and spiral scanning, with low pitch and retrospective gating.

CANCER RISK

The **Figure** shows the estimates of the excess lifetime risk of radiation-induced cancer from a single CAC CT scan according to age at screening. The estimated risks decreased with increasing age at screening for all protocols primarily because of the reduced life expectancy. For the median dose of 2.3 mSv (range, 0.8-10.5 mSv), a single screening at the age of 40 years was estimated to result in a lifetime excess cancer risk of 9 (range, 3-42) and 28 (range, 9-130) cancers per 100 000 persons for men and women, respectively. This risk decreased to 3 (range, 1-13) (for men) and 6 (range, 2-26) (for women) per 100 000 persons from screening at the age of 80 years.

The largest proportion of the total radiation-induced cancer incidence, 72% and 71% for men and women, respectively, was attributable to lung cancer, followed by breast cancer for women (20%), and then leukemia (12% and 4% for men and women, respectively) (**Table 3**). The estimated risk from all cancers combined was higher for women than for men because of the contribution from radiation-induced breast cancer and also because the risk of radiation-induced lung cancer was estimated to be about 2-fold higher for women than for men. Assuming screening every 5 years from age 45 to 75 years for men and 55 to 75 years for women, the cumulative radiation-induced cancer risk from the median dose of 2.3 mSv (range, 0.8-10.5 mSv) was estimated to be 42 per 100 000

Table 3. Site-Specific Estimates of the Lifetime Risk of Radiation-Induced Cancer From a Single Coronary Artery Calcification Computed Tomographic Screen at Age 55 Years

Type of Cancer	Radiation-Induced Cancer Incidence, per 100 000 Persons, No. (%) ^a	
	Men	Women
Breast		4 (20)
Lung	6 (72)	14 (71)
Leukemia	1 (12)	1 (4)
Other solid cancers	1 (15)	1 (6)
Total	8 (100)	20 (100)

^aSite-specific risks were estimated based on organ dose estimates associated with a median effective dose of 2.3 mSv.

for men (range, 14-200) and 62 per 100 000 for women (range, 21-300).

COMMENT

We observed a more than 10-fold variation in radiation doses from CAC screening with MDCT and therefore wide variation in the estimated radiation-induced cancer risk. The range of estimated effective doses is similar to the range from a recent literature review (range, 1.0-12 mSv; mean, 3.0 mSv).⁴⁰ Many factors influence the radiation dose from medical radiation sources. For CAC CT, these include the CT scanner model, scan mode, electrocardiographic triggering or gating, x-ray tube potential (kilovolt peak [kVp]), tube current-time product (mAs), pitch,^{41,42} and scan length. Even for the same CT scanner model, CT scan technique or parameter settings may vary between hospitals. For example, there are 3 different protocols in Table 1 for the Volume Zoom CT scan-

ner. Despite the fact that the current-time products were similar for these 3 protocols (range, 50-55 mAs), the estimated effective radiation doses varied from 1.3 to 3.1 mSv. The higher estimates were primarily attributable to the use of higher tube potential or spiral scanners with a lower pitch.

Slower gantry speed and retrospective gating were the main explanations for the higher radiation exposures in some of the protocols (eg, study 1, LightSpeed QX/i scanner). Because of the intrinsic slower gantry speed, 2 full gantry rotations are necessary to create an image during the desired phase of the cardiac cycle.²² Also, retrospective gating results in the x-ray beam being turned on during the whole rotation time. Both features result in an extended exposure time of 1.6-second per imaging level and thus a higher radiation dose, whereas exposure times for the other protocols ranged from 0.2 to 0.5 seconds. Low pitch and retrospective gating also yielded relatively high radiation doses (eg, study 4, Sensation 64 and Volume Zoom scanners). Radiation dose is also inversely proportional to pitch, and a low pitch factor, typically between 0.2 and 0.375, is used for spiral scanning for cardiac CT.

The radiation dose increases rapidly with kVp (as a rule of thumb, radiation dose is proportional to kVp with power of 2.5⁴³). The study 1 protocol for the Volume Zoom scanner uses 140 kVp, while most other protocols we reviewed recommend 120 kVp (Table 1). The higher kVp resulted in an estimated effective dose for this protocol that was about 70% higher than the otherwise similar protocol for the same scanner (study 4, axial scan). The radiation dose is linearly proportional to the tube current time product (mAs). Two of the university hospital protocols in our study use the same Siemens Definition scanner but differ considerably in radiation dose owing to the different mAs used for imaging (protocols from hospitals 2 and 3). The same mAs will result in a higher radiation dose⁴⁴ and less image noise for smaller patients owing to less radiation attenuation by less tissue. Some protocols suggest reducing the mAs for small patients (Table 1), although, in practice, most CT technologists use a default protocol for calcium scoring, adjusting just the scan area to cover from the carina to below the cardiac apex.

The differences in dose observed between scanners and protocols highlights the importance of using scanner equipment that enables a low-dose scan to be performed and of optimizing protocols for a specific scanner model. These considerations are even more important when the CT scan is being used for screening a population that will mostly involve healthy individuals. Moreover, the broader the population that is to be scanned (SHAPE proposes screening approximately 50 million Americans), the greater the potential impact in terms of attributable cancer from a small increase in radiation dose. Therefore, it is essential to optimize calcium scoring protocols to minimize dose while maintaining adequate image quality to yield a reliable calcium score. The wide variation in the protocols reviewed herein also highlights the fact that there are still no agreed-on standard protocols for CAC quantification by MDCT. While the International Consortium has recently recommended that protocols should be standardized, to date it has only

published protocols for a limited number of scanners, including few current-generation scanners.²⁴ Further efforts by professional societies are necessary to standardize protocols.

Diamond and Kaul⁴⁵ have performed cost-effectiveness analyses of the SHAPE paradigm in comparison with other cardiovascular prevention approaches. They estimated that 1-time screening of 50 million individuals could, assuming perfect statin adherence in patients with high CAC, prevent 24 000 deaths and 96 000 nonfatal cardiovascular events, at a net cost of \$17 billion, equivalent to \$32 000 per life-year equivalent saved in comparison to a standard prevention strategy based on National Cholesterol Education Program guidelines.⁴⁶ Assuming that 50 million individuals in the United States in the age group had a single screening with 1 of the protocols with the median radiation dose of 2.3 mSv (hospital 1, second protocol), our estimates suggest that the single screening could result in about 5600 individuals (range, 2700-37 000 individuals depending on CT protocol) developing a radiation-induced cancer in the future. Estimates of the radiation-induced cancers were not included in the cost-effectiveness calculations described above. These calculations also provide an informal indication of how the radiation risks might compare with the potential benefits under the best case scenario of 100% treatment compliance.

There are a number of sources of uncertainty in radiation risk estimates owing to the lack of precision in the parameter estimates and uncertain assumptions, such as the form of the dose-response relationship at low doses. In the present study, the extrapolation was performed under the linear no-threshold assumption, with a dose and dose-rate effectiveness factor of 1.5. However, there is also epidemiological and radiobiological evidence that supports both downwardly and upwardly curving slopes, and these alternatives to the BEIR VII risk models would result in higher or lower risk estimates, respectively.⁵

Another uncertainty involved in radiation risk assessment is the transfer of risk models estimated from the Japanese to other populations with different background cancer rates. The BEIR VII committee's approach to this uncertainty was to use a weighted average of 2 risk models with different underlying assumptions: the excess relative risk model, which is based on the assumption that the risk from radiation exposure multiplies the background cancer risk in the population, and the absolute excess risk model, which is based on the assumption that the risk from radiation exposure adds to the background cancer risk in the population. Although we have not calculated formal confidence bounds for our radiation risk estimates, the BEIR VII committee did conduct such calculations for the risk of all cancers combined, and their results suggest that combination of the uncertainty in the dose and dose-rate effectiveness factor, the transport of the risk models from the Japanese to the US population, and the radiation risk coefficients could mean that the projected cancer risks for each protocol could be higher or lower than our point estimates by a factor of 2.³³

We reviewed protocols and estimated radiation doses and associated cancer risks from CAC screening with

MDCT. These risks can be compared with estimates of the benefits from such screening once they are available so as to design appropriate screening and prevention strategies for coronary artery disease. There have been no widely agreed-on standard protocols for CAC screening by MDCT. Radiation doses and relevant radiation-induced cancer risks vary depending on protocols up to an order of magnitude. Many technical factors influence radiation dose from CAC measurement with MDCT. Careful optimization of these factors may reduce radiation exposure without detriment to the clinical purpose of the screening examination. Further efforts by professional societies are necessary to standardize protocols in order to decrease unnecessary radiation exposure and to minimize cancer risk.

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Correction

Error in Text. In the Review Article by Myung et al titled "Effects of Web- and Computer-Based Smoking Cessation Programs: Meta-analysis of Randomized Controlled Trials," published in the May 25, 2009, issue of the *Archives* (2009;169[10]:929-937), the 95% confidence intervals for the relative risks throughout the text should not have been presented as percentages, for example, not 1.27%-1.64% but rather 1.27-1.64.