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Radiation-related cancer risks from CT colonography screening: a risk-benefit analysis

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Abstract

Objective—The purpose of this study was to estimate the ratio of cancers prevented to induced (benefit-risk ratio) for CT colonography screening every five years from age 50-80.

Materials and methods—Radiation-related cancer risk was estimated using risk projection models based on the National Research Council's BEIR VII committee's report and screening protocols from the American College of Radiology Imaging Network's National CT Colonography Trial. Uncertainty limits (UL) were estimated using Monte-Carlo simulation methods. Comparative modelling with three colorectal cancer microsimulation models was used to estimate the potential reduction in colorectal cancer cases and deaths.

Results—The estimated mean effective dose per CT colonography screen was 8mSv for females and 7mSv for males. The estimated number of radiation-related cancers from CT colonography screening every 5 years from age 50-80 was 150 cases/100,000 individuals (95%UL:80-280) for males and females. The estimated number of colorectal cancers prevented by CT colonography every 5 years from age 50-80 ranged across the three microsimulation models from 3580 to 5190/100,000, yielding a benefit-risk ratio that varied from 24:1(95%UL=13:1-45:1) to 35:1(95%UL=19:1-65:1). The benefit-risk ratio for cancer deaths was even higher than the ratio for cancer cases. Inclusion of radiation-related cancer risks from CT scans following-up extracolonic findings did not materially alter the results.

Conclusions—Concerns have been raised about recommending CT colonography as a routine screening tool because of the potential harms, including the radiation risks. Based on these models the benefits from CT colonography screening every five years from age 50-80 clearly outweigh the radiation risks.

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Introduction

Clinical trial results show that computed tomographic (CT) colonography can be as sensitive as optical colonoscopy for the detection of large adenomatous polyps and colorectal cancers (1). However, recent updates to colorectal cancer screening guidelines in the US make conflicting recommendations about the use of CT colonography. The American Cancer Society concluded that there was now sufficient evidence to recommend it as a routine screening tool (2), while the United States Preventive Services Task Force did not recommend it for screening, because of concerns about the balance of the benefits and the harms (3). Medicare recently cited similar concerns as part of the basis for the decision not to provide reimbursement for this screening modality (4). The potential harms highlighted in these reports include the risks from procedures associated with extra-colonic findings as well as the potential risk of radiation-related cancer from repeated CT screening and from follow-up CT scans for the extracolonic findings.

It is generally regarded as infeasible to study the risk of radiation-related cancer from screening CT scans directly. For example, one would need to follow approximately 100,000 individuals for their lifetimes in order to detect a significantly increased cancer risk after radiation exposure equal to the expected exposure from CT colonography screening every 5 years from age 50-70 years (5). A more timely and practical assessment of the potential radiation risks can be estimated using risk projection models. In a previous study using this approach the cancer risk from radiation exposure from a single CT colonography at age 50 was estimated to be about 0.14% (6).

The aim of the current study was to estimate and compare the lifetime risk of radiation-related cancer from repeated CT colonography screening with the number of colorectal cancers prevented by screening. We used updated risk models developed by the National Research Council's BEIR VII committee (Biological Effects of Ionising Radiation) to estimate the radiation-related cancer risk (7). We estimated the potential reduction in colorectal cancer incidence from CT colonography screening using comparative modelling with three microsimulation models of colorectal cancer (8), and then calculated the benefit-risk ratio according to age at initial screening. We also estimated the potential risk of radiation-related cancer from follow-up CT scans performed due to extracolonic findings detected during screening CT colonography.

Methods

Radiation dose estimation

We used the protocol from the recent American College of Radiology Imaging Network's (ACRIN) National CT Colonography Trial to estimate organ and sex-specific radiation doses. The protocol was developed for nine multi-detector CT scanners that had a minimum of 16 rows (16, 40, and 64 rows) (9). Technical parameters specified in the protocol were 120 kVp, slice collimation of 1.0-1.25 mm, and pitch of 0.98-1.5. These parameters plus tube current-time products (mAs) for a medium-size patient (50 mAs) were used in the computer software CT-Expo (10) to estimate the organ doses. We calculated the mean organ doses across nine scanner types for use in the risk estimation and also calculated effective dose estimates for comparison with previous publications (11). Since CT colonography screening generally involves two scans (i.e., one with the patient in the supine position and one in the prone position) doses were estimated based on a paired examination (9).

Radiation risk estimation

We estimated the risk of radiation-related cancer from a single CT colonography screen at age 40, 50, 60, and 70 and also from repeated screening every five years starting at age 40,

50 or 65 and ending at age 80. For repeated screening we assumed that the number screened at each screening round depended on surviving to that age without having been diagnosed with colorectal cancer and on having no findings detected on a previous CT colonography scan. Individuals with positive CT colonography scans were assumed to undergo subsequent screening or surveillance with colonoscopy (see below).

To estimate the radiation risks we developed organ-specific radiation risk models for the US population for each of the organs estimated to receive radiation exposure from CT colonography screening (Table 1). These models were based on the BEIR VII committee's approach to site-specific risk estimation (7) (Appendix 1). Most of the models were developed using cancer incidence data from the latest follow-up of the Japanese atomic bomb survivors because these are the most detailed data available for these sites (12,13). The exceptions were breast and thyroid cancer, for these sites the models were based on pooled analysis of medically exposed populations and the Japanese atomic bomb survivors (7). For solid cancers we assumed that the risk was linear in dose and for leukemia that the dose-response model was linear-quadratic.

The cancer risk calculations were performed using Analytica software (14), which employs Monte Carlo simulation methods to estimate risks with uncertainty intervals, accounting for statistical uncertainties in the risk parameters and subjective uncertainties in the risk model assumptions (including the dose and dose rate reduction effectiveness factor and method for transferring risks from the Japanese to the US population) by assigning distributions to these parameters. In each of 1000 simulations the parameters were sampled randomly from their assigned distributions and the risk re-calculated, resulting in a distribution of potential results. We report the mean estimates from the simulations with 95% uncertainty limits (95% UL).

To estimate the number of radiation-related cancer deaths we multiplied the estimated number of radiation-related cancer cases by the proportion of these cancers that typically result in death. We estimated this proportion for each cancer using the ratio of the current US age-standardized cancer mortality rate compared to the current age-standardized cancer incidence rate (15). The total cancer risk was estimated by summing across all exposed sites.

Additional CT scans for extracolonic findings

Several studies have tracked the number of follow-up examinations for extracolonic findings (16-18). We estimated the mean frequency of each type of follow-up CT scan (whole body, abdomen/pelvis and chest CT) from these studies and then estimated the associated organ-doses using typical CT parameters (mAs, kVp etc) for each scan type from a national survey that obtained data on technique factors from 256 randomly-selected CT facilities in the US (19) and CT-Expo software (10). Age and sex-specific risks of radiation-related cancer for these scan types were then estimated using the methods described above for the screening scans. As no information is available on follow-up scans from repeated screening we assumed that the frequency was the same after each screening round.

Microsimulation models of the screening benefit

We estimated the number of colorectal cancer cases and deaths averted by CT colonography screening using three independently-developed microsimulation models of the National Cancer Institute's Cancer Intervention and Surveillance Modeling Network (CISNET) consortium: MISCAN, SimCRC, and CRC-SPIN. These models were previously used to assess the cost-effectiveness of CT colonography screening for colorectal cancer in the Medicare population (8). Standardized profiles of each model's structure, assumptions, and calibration methods are available at http://cisnet.cancer.gov/profiles/. Each model simulates

the life histories of a large population of individuals from birth to death and has a natural history component that tracks the progression of colorectal disease in the absence of screening. At each simulated age one or more adenomas may develop. Adenomas may grow in size and some may become malignant. A preclinical (i.e., undetected) cancer has a chance of progressing through stages I to IV and may be detected by symptoms at any stage. Survival following diagnosis was estimated using SEER data (15).

Test Characteristics

Each model also has a screening mechanism that simulates the ability of CT colonography to detect adenomas or preclinical cancer based on its sensitivity for that lesion. CT colonography test characteristics were derived from the published report on the ACRIN National CT Colonography Trial (1). Sensitivity was 57% for a 6-9 mm adenoma and 84% for an adenoma 10 mm or larger. We assumed the sensitivity for cancer was the same as that for large adenomas. Sensitivity estimates for diagnostic and surveillance colonoscopies were derived from a meta analysis and were 75% for an adenoma less than 6 mm, 85% for a 6-9 mm adenoma, and 95% for an adenoma 10 mm or larger or for cancer (20). The models use these adenoma-specific sensitivities to simulate detection of adenomas and preclinical cancers by either CT colonography or colonoscopy.

Screening, Follow-up, Surveillance, and Adherence Assumptions

To estimate the reduction in colorectal cancer incidence and mortality due to CT colonography screening, the three CISNET models predicted colorectal cancer incidence and mortality rates when there is no screening and with CTC screening every five years starting at age 40, 50 or 65 and ending at age 80. We assumed individuals with findings 6 mm or larger on CT colonography were referred for diagnostic follow-up with optical colonoscopy. If no adenomas or cancer were detected at follow-up, the person was assumed to undergo subsequent screening with colonoscopy every 10 years (as long as no adenomas or cancer were detected at subsequent colonoscopies). Individuals with adenomas that were detected and removed by colonoscopy were assumed to undergo colonoscopy surveillance per guidelines, i.e. every 3 years among individuals with an adenoma 10 mm or larger or with 3 or more adenomas of any size detected at the last colonoscopy, and every 5 years otherwise. We assumed surveillance continued until the diagnosis of colorectal cancer or death and individuals were 100% adherent with screening, follow-up, and surveillance procedures.

The number of colorectal cancer cases and deaths prevented by screening was estimated by subtracting the results for the model runs that included screening from those without screening. For example, the additional benefit from starting screening at age 50 rather than age 65 was estimated by subtracting the number of colorectal cancer cases and deaths prevented by screening from age 65-80 from those for screening from age 50-80. This gives the additional benefit from screening age 50-64 assuming that screening continues through age 80.

Results

The mean organ dose estimates for a single screen varied from 1mGy to the breast to 13mGy to the kidneys and stomach (Appendix 2). A number of organs were estimated to receive doses of approximately 10mGy (pancreas, stomach, liver, colon, bladder, kidney, and ovary). The estimated mean effective dose was 8mSv for females and 7mSv for males.

The estimated number of radiation-related cancers from a single CT colonography screen for females at age 50 was 55 per 100,000 screens (95%UL:28-100) (Table 1). The largest

contributions to the total cancer risk were from colorectal cancer (n=12 (3-29)) and bladder cancer (n=12 (3-29)). The estimated risks were similar for a single screen at age 40 and halved for a screen at age 70 (30 cancers per 100,000 (20-60), data not shown) because of shorter life-expectancy. Results were broadly similar for males and so subsequent analyses were conducted for males and females combined.

The radiation-related cancer risk from repeated CT colonography screening every five years from age 50-80 was estimated to be 150 cases (95%UL:80-280) per 100,000 screened (Table 2). The estimated number of colorectal cancers prevented by CT colonography screening for the same screening period ranged across the three microsimulation models from 3580 to 5190 per 100,000, giving a benefit-risk ratio that varied from 24:1 (95%UL=13:1-45:1) to 35:1 (95%UL=19:1-65:1). The benefit-risk ratio was considerably larger for screening from age 65-80 than for additional screening from age 50-64, but the ratios were greater than 1:1 across all three models. The benefit-risk ratio for the additional benefit from screening age 40-49 for the MISCAN model was only 1.5:1 with a lower uncertainty limit of 0.8:1, the ratio for the two other models was also quite low.

The benefit-risk ratio for cancer deaths was higher than the ratio for cancer incidence, but followed a similar pattern across ages and microsimulation models (Table 3).

The estimated number of CT scans performed to investigate extracolonic findings detected by screening ranged from 2900 to 12,500 per 100,000 individuals (Table 4). The additional radiation-related cancer risk from these scans varied from 2.5-7 cancers per 100,000 individuals after a screen at age 50 (Table 4), and from 1-4 after a screen at age 70 (data not shown). Based on these estimates the total additional cancers from follow-up CT scans after screening from age 50-80 was in the range 15-35 cancers per 100,000 screened. This additional risk had only a small impact on the benefit-risk ratio. For example, assuming 35 additional cancers from the follow-up scans reduced the mean benefit-risk ratio from 24:1 to 19:1 for screening age 50-80 using the MISCAN model.

Discussion

Several organizations have raised concerns about the radiation risks from CT colonography screening and requested additional research be conducted in this area (3,4). We used updated risk projections models and microsimulation models to estimate the benefit-risk ratio for radiation risks from repeated CT colonography screening. The benefits from screening every five years age 50-80 were estimated to clearly outweigh the radiation-related cancer risks. Inclusion of the radiation-related risk from CT scans used to follow-up extracolonic findings did not materially alter these findings.

We used the National CT Colonography trial protocol (7) to estimate the mean effective dose estimates associated with CT colonongraphy and the sensitivity of CT colonography was also based on the results from this trial, ensuring directly comparable estimation of benefits and risks. The protocols should also be reasonably representative of current screening practice in the US since the trial included a variety of community and academic sites using 16+ slice multi-detector CT scanners (1,22). Our dose estimates were also similar to the mean dose for the US in a recent review of international CT colonography screening protocols (7-8mSv versus 6.7mSv) (21) and in line with recent recommendations by the American College of Radiology (23). Variation in doses across scanner types (Appendix 2) is likely due to differences in x-ray beam intensity and beam spectrum (24). It has been suggested that radiation doses from CT colonography could be reduced further (25,26). However, to date these low-dose protocols do not seem to have been widely adopted, possibly due to a reluctance to accept lower image quality.

A previous radiation risk projection study by Brenner and Georgsson estimated that the risk of radiation-related cancer from CT colonography screening was more than two-fold higher than our mean estimate (0.14% for a single screen at age 50 compared to 0.06%) (6). Our organ-specific dose estimates were broadly similar to those used by Brenner and Georgsson. The differences between the risk estimates are due primarily to different assumptions regarding risk transfer from the Japanese to the US population in the recent BEIR VII report (used here) compared to the previous BEIR V report (used by Brenner and Georgsson) (7,27). Detailed discussion of these assumptions is beyond the scope of this paper but is covered in detail in the BEIR VII report (7). The upper uncertainty bounds for our radiation risk estimates correspond (approximately) to the assumptions in the BEIR V report. Even using the upper uncertainty bounds of the risk estimates the benefit-risk ratio was 4:1 or higher for screening from age 50-80. A recent cost-effectiveness analysis for CT colonography screening (28) incorporated these earlier radiation risk estimates (6). Unfortunately the estimate of lifetime cancer risk used was incorrect by a factor of ten (0.01% instead of 0.1%). No other published studies have provided the information in the form necessary to conduct a direct comparison of the radiation risks and benefits from repeated CT colonography screening.

A number of studies have shown that 5-10% of asymptomatic screening patients will have a clinically significant extracolonic finding on CT colonography screening (16-18). There are potential benefits from these findings such as the visualization of abdominal aortic aneurysms (29) but there are also additional risks, including an additional risk of radiation-related cancer from follow-up CT scans. We were only able to conduct crude calculations for these follow-up scans due to limited available data. In particular we had no data on the follow-up of extracolonic findings after the first screening round, which may be lower if previously observed findings are not referred for additional follow-up. Despite our probable over-estimation of the risks associated with follow-up scans, our results suggest that the additional radiation risk from these scans is unlikely to significantly alter the overall benefit-risk ratio.

Very large studies with lifelong follow-up would be required to accurately and directly quantify risks from low-dose radiation exposures like CT colonography screening (5), which is why we used an indirect modeling approach to provide a more timely estimate of the potential risks based on existing data. There is an ongoing scientific debate about the linear no-threshold assumption, which forms the basis for these risk projections (29). This assumption is that there is no dose below which there is no risk of radiation-related cancer and that the risk at low doses is approximately linear. Most national and international radiation protection organizations support the use of this assumption for the purpose of radiation protection (7,30,31). Although there is evidence of excess cancer risks from low-dose exposures in studies of the Japanese atomic bomb survivors, nuclear workers and patients exposed to multiple diagnostic X-rays (7) many uncertainties remain including the magnitude of the effects at low doses and the effects of single acute exposures compared to fractionated exposures or protracted exposures. Risk projection methods can help to quantify the potential risk, but because of the uncertainties these methods require a number of assumptions.

An important strength of our study was the use of Monte Carlo simulation methods to quantify the uncertainties in the radiation risk estimates ; this allowed us to examine the benefit-risk ratio at the extremes of the radiation risk limits. However, there are other uncertainties and assumptions involved in such risk projections that were not included in the uncertainty intervals, such as uncertainty about the biological effectiveness of low energy X-rays in terms of cancer induction. We assumed that they are equally effective as higher energy gamma rays, the primary exposure from the Japanese atomic bombs. It is possible

that they may be more carcinogenic, which would mean that our projections would underestimate the cancer risks, possibly by a factor of two (7). A possible source of overestimation of the risks is that some colorectal cancers that are related to the radiation from the CT colonography screening may be detected at future screening rounds. Furthermore, our results assume screening is performed every 5 years; some recent guidelines suggest that it could be conducted every 10 years (32). This would reduce the radiation risks presented here by approximately 50%.

No direct estimates of the colorectal cancer incidence or mortality reductions from CT colonography screening are currently available. To date the randomized trials have only assessed surrogate markers for efficacy, primarily screening sensitivity (1). Our estimates of the number of colorectal cancers prevented by screening varied between the three microsimulation models primarily because of the differences in the assumed dwell time (the amount of time between onset of an adenoma and clinical presentation of colorectal cancer). The comparative modelling was another strength of the current study, and despite differences in estimated disease reduction, the conclusions were qualitatively similar for all three models. These analyses provide a plausible range for expected results, but do not provide information about the precision of the estimated benefit of CT colonography. The uncertainty limits for estimated benefit:risk ratios only account for uncertainty in the estimated risk, and therefore underestimate the overall uncertainty of this ratio.

It is unlikely that there will be direct estimates of either the radiation risks or the number of cancers prevented by CT colonography screening in the near future. In the absence of direct evidence, this modelling approach, which was based on the best available current data, suggests that after age 50 the benefits clearly outweigh the radiation risks from CT colonography screening. The estimated risk of radiation-related cancer per screen is small, <0.1%, especially when compared to the typical background lifetime risk of developing cancer of about 40% (33). Screening is not generally recommended for the general population before age 50 (2,3), and our results suggest that the absolute benefit may not be much greater than the radiation risk for screening age 40-49. Our estimates can be used to help inform the overall risk-benefit assessment of CT colonography in comparison with alternative colorectal cancer screening options.

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Appendix

Appendix 1

Coefficients for the radiation risk models for site-specific solid cancer incidence (based on the BEIR VII risk models (7) and Preston et al (12,13))

	ERR model				EAR model			
Cancer site	**B - males**	**B - females**	**H**	**J**	**B - males**	**B - females**	**H**	**J**
Stomach	0.21	0.48	-0.3	-1.4	4.9	4.9	-0.41	2.8
Colon	0.63	0.43	-0.3	-1.4	3.2	1.6	-0.41	2.8
Liver	0.32	0.32	-0.3	-1.4	2.2	1	-0.41	4.1
Pancreas*	0.36	0.36	-0.3	-1.4	0.49	0.49	-0.41	2.8
Lung	0.32	1.4	-0.3	-1.4	2.3	3.4	-0.41	5.2

	ERR model				EAR model			
Cancer site	**B - males**	**B - females**	**H**	**J**	**B - males**	**B - females**	**H**	**J**
Prostate	0.12	-	-0.3	-1.4	0.11	-	-0.41	2.8
Breast†	-	-	-	-	-	9.4	-0.51	3.5, 1.1
Ovary	-	0.38	-0.3	-1.4	-	0.7	-0.41	2.8
Uterus	-	0.055	-0.3	-1.4	-	1.2	-0.41	2.8
Bladder	0.5	1.65	-0.3	-1.4	1.2	0.75	-0.41	6
Kidney*	0.34	0.34	-0.3	-1.4	0.31	0.31	-0.41	2.8

The excess relative risk (ERR) or excess absolute risk (EAR) are of the form B_S D exp [H. e*] $(a/60)^J$ where D is the dose in Gy, e is age at exposure in years, e* is (e-30)/10 for e <30 and zero for e ≥ 30, and a is attained age in years (7).

Lifetime risk was calculated as a weighted average of the excess relative risk (ERR) and the excess absolute risk (EAR) model (weighted on the linear scale).

For most cancer sites a weight of 0.7 was used for the ERR model and 0.3 for the EAR model. The exceptions were: lung (EAR=0.7 and ERR=0.3) and breast (ERR=0 and EAR=1).

A dose and dose rate reduction effectiveness factor with an average value of 1.5 was included for doses <100mGy(7).

A five year lag period was assumed for solid cancers and two years for leukaemia(7).

*These cancer sites were not included in the BEIR VII report but the models were developed using the approach from the BEIR VII report.

†The breast cancer risk model is from Preston et al (2002)(13). The attained age parameters are for attained age less than 50 and 50+, respectively.

Appendix

Appendix 2

Organ-specific radiation dose estimates (mGy) from a single CT colonography screen

a) Females

	Manufacturer and CT scanner									
Organ	**GE 16 Slice**	**GE 64 Slice**	**Siemens 16 Slice**	**Siemens 64 Slice**	**Toshiba 16 Slice**	**Toshiba 64 Slice**	**Philips 16 Slice**	**Philips 40 Slice**	**Philips 16 Slice**	**Mean**
Stomach	15	14	13	10	17	16	11	9	8	13
Colon	14	13	12	10	16	15	10	8	8	12
Liver	14	14	12	10	17	16	10	9	8	12
Pancreas	12	12	11	8	14	14	9	7	7	10
Lung	2	3	2	2	3	6	2	2	2	3
Breast	1	1	1	1	1	5	1	1	1	1
Ovary/uterus	14	13	12	9	16	14	10	8	7	11
Bladder	15	14	13	10	17	16	11	9	8	12
Kidney	16	15	13	11	18	17	11	9	8	13
Bone marrow	7	7	6	5	8	8	5	4	4	6
Effective Dose (mSv)	10	9	8	7	11	11	7	6	5	8

b) Males

	Manufacturer and CT scanner									
Organ	GE 16 Slice	GE 64 Slice	Siemens 16 Slice	Siemens 64 Slice	Toshiba 16 Slice	Toshiba 64 Slice	Philips 16 Slice	Philips 40 Slice	Philips 16 Slice	Mean
Stomach	15	14	12	10	17	16	10	9	8	12
Colon	14	13	12	9	16	14	10	8	7	11
Liver	14	13	12	9	16	15	10	8	8	12
Pancreas	11	11	10	8	13	13	8	7	6	10
Lung	2	2	2	1	3	5	1	1	2	2
Prostate	4	9	5	5	9	15	3	5	7	7
Bladder	14	13	12	9	16	15	10	8	8	12
Kidney	15	14	13	10	17	16	11	9	8	13
Bone marrow	6	6	5	4	7	7	5	4	4	5
Effective Dose (mSv)	7	8	6	5	9	10	5	5	5	7

References

1. Johnson CD, Chen MH, Toledano AY, et al. Accuracy of CT colonography for detection of large adenomas and cancers. N Engl J Med. 2008; 359(12):1207–17. [PubMed: 18799557]
2. Levin B, Lieberman DA, McFarland B, et al. Screening and surveillance for the early detection of colorectal cancer and adenomatous polyps, 2008: a joint guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology. CA Cancer J Clin. 2008; 58(3):130–60. [PubMed: 18322143]
3. Screening for colorectal cancer: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med. 2008; 149(9):627–37. [PubMed: 18838716]
4. Decision memo for screening computed tomography (CTC) for colorectal cancer (CAG-00396N). (Accessed date: May 15th 2009). for Medicare and Medicaid Services (CMS) 2009.
5. Land CE. Estimating cancer risks from low doses of ionizing radiation. Science. 1980; 209(4462): 1197–203. [PubMed: 7403879]
6. Brenner DJ, Georgsson MA. Mass screening with CT colonography: should the radiation exposure be of concern? Gastroenterology. 2005; 129(1):328–37. [PubMed: 16012958]
7. Committee to assess health risks from exposure to low levels of ionizing radiation National Research Council. (National Academy of Sciences). Health risks from exposure to low levels of ionizing radiation. BEIR VII; 2005.
8. Knudsen AB, Lansdorp-Vogelaar I, Rutter CM, et al. Cost-Effectiveness of Computed Tomographic Colonography Screening for Colorectal Cancer in the Medicare Population. J Natl Cancer Inst. Jul 27.2010 [Epub ahead of print].
9. ACRIN. [2009 Jan 10] (Available from:http://www.acrin.org/TabID/151/Default.aspx.). ACRIN Protocol 6664: The national CT colonagraphy trail
10. Stamm G, Nagel HD. [CT-expo--a novel program for dose evaluation in CT]. Rofo. 2002; 174(12): 1570–6. [PubMed: 12471531]
11. ICRP (International Commission on Radiological Protection). (Ann ICRP 21 (1-3)). 1990 recommendations of the international commission on radiological protection. 1991.
12. Preston DL, Ron E, Tokuoka S, et al. Solid cancer incidence in atomic bomb survivors: 1958-1998. Radiat Res. 2007; 168(1):1–64. [PubMed: 17722996]
13. Preston DL, Mattsson A, Holmberg E, Shore R, Hildreth NG, Boice JD Jr. Radiation effects on breast cancer risk: a pooled analysis of eight cohorts. Radiat Res. 2002; 158(2):220–35. [PubMed: 12105993]

14. Analytica 4.1. Lumina Decisions Systems Inc.; 2008. program
15. SEER. (Surveillance, Epidemiology and End Results). SEER*Stat Database: Incidence - SEER 17 regs. National Cancer Institute (U.S.). Division of Cancer Control and Population Sciences, Surveillance Research Program Cancer Statistics Branch; 2006.
16. Pickhardt PJ, Hanson ME, Vanness DJ, et al. Unsuspected extracolonic findings at screening CT colonography: clinical and economic impact. Radiology. 2008; 249(1):151–9. [PubMed: 18796673]
17. Yee J, Kumar NN, Godara S, et al. Extracolonic abnormalities discovered incidentally at CT colonography in a male population. Radiology. 2005; 236(2):519–26. [PubMed: 16040909]
18. Gluecker TM, Johnson CD, Wilson LA, et al. Extracolonic findings at CT colonography: evaluation of prevalence and cost in a screening population. Gastroenterology. 2003; 124(4):911–6. [PubMed: 12671887]
19. National Evaluation of X-ray trends (NEXT). Tabulation of graphical summary of 2000 survey of computed tomography. 2007.
20. van Rijn JC, Reitsma JB, Stoker J, Bossuyt PM, van Deventer SJ, Dekker E. Polyp miss rate determined by tandem colonoscopy: a systematic review. Am J Gastroenterol. 2006; 101(2):343–50. [PubMed: 16454841]
21. Liedenbaum MH, Venema HW, Stoker J. Radiation dose in CT colonography--trends in time and differences between daily practice and screening protocols. Eur Radiol. 2008; 18(10):2222–30. [PubMed: 18491095]
22. Macari M, Bini EJ, Xue X, et al. Colorectal neoplasms: prospective comparison of thin-section low-dose multi-detector row CT colonography and conventional colonoscopy for detection. Radiology. 2002; 224(2):383–92. [PubMed: 12147833]
23. American College of Radiology. ACR practice guideline for the performance of computed tomography (CT) colonography in adults. Res. 2009; 36 http://acr.org/.../guidelines/dx/gastro/ct_colonography.aspx.
24. Nagel, HD. Radiation dose from adults and pediatric multidetector computed tomography. Springer; Berlin, Germany: 2007. CT parameters that influence the radiation dose.; p. 51-79.
25. Cohnen M, Vogt C, Aurich V, Beck A, Haussinger D, Modder U. Multi-slice CT-colonography in low-dose technique--Preliminary results. Rofo. 2002; 174(7):835–8. [PubMed: 12101472]
26. Iannaccone R, Catalano C, Mangiapane F, et al. Colorectal polyps: detection with low-dose multi-detector row helical CT colonography versus two sequential colonoscopies. Radiology. 2005; 237(3):927–37. [PubMed: 16304113]
27. Committee on the Biological Effects of Ionizing Radiation (BEIR V) National Research Council. (National Academy of Sciences). Health effects of exposure to low levels of ionizing radiation. BEIR V; 1990.
28. Hassan C, Pickhardt PJ, Laghi A, et al. Computed tomographic colonography to screen for colorectal cancer, extracolonic cancer, and aortic aneurysm: model simulation with cost-effectiveness analysis. Arch Intern Med. 2008; 168(7):696–705. [PubMed: 18413551]
29. Little MP, Wakeford R, Tawn EJ, Bouffler SD, Berrington de Gonzalez A. Risks associated with low doses and low dose rates of ionizing radiation: why linearity may be (almost) the best we can do. Radiology. 2009; 251(1):6–12. [PubMed: 19332841]
30. International Commission on Radiological Protection. (Report No.: ICRP Publication 99 Contract No: 4). Low - Dose Extrapolation of Radiation Related Cancer Risk. 2006.
31. United Nations Scientific Committee on the Effects of Atomic Radiation. (United Nations). Sources and effects of ionizing radiation. 2006.
32. Zalis ME, Barish MA, Choi JR, et al. Working Group on Virtual Colonoscopy. CT colonography reporting and data system: a consensus proposal. Radiology. 2005; 236(1):3–9. [PubMed: 15987959]
33. Fast Stats: An interactive tool for access to SEER cancer statistics. Surveillance Research Program, National Cancer Institute; http://seer.cancer.gov/faststats.

Table 1

Estimated mean (and 95% UL) risk of radiation-related cancer incidence (per 100,000 screened) following a single CT colonography screen at age 50: according to cancer type

	Females		Males	
Cancer site	**(per 100,000)**	**(95% UL)**	**(per 100,000)**	**(95% UL)**
Stomach	8	(1-28)	6	(1-25)
Colorectal	12	(3-29)	16	(6-35)
Other digestive †	5	(0-19)	6	(1-26)
Lung	7	(3-20)	3	(1-6)
Breast	1	(1-2)	-	-
Ovary	3	(1-10)	-	-
Uterus	2	(0-10)	-	-
Prostate	-	-	9	(0-41)
Bladder	12	(3-29)	12	(3-32)
Kidney	2	(0-7)	3	(0-12)
Leukemia	4	(1-11)	5	(1-13)
Total	55	(28-100)	59	(28-104)

† Liver, gallbladder and pancreatic cancer.

Table 2

Comparison of the estimated number of radiation-related cancers with the number of colorectal cancers prevented by CT colonography screening every five years (per 100,000): according to microsimulation model and age at screening

Microsimulation model	Age at screening	Average no. of screens (per person)	Colorectal cancers prevented	Radiation-induced cancer incidence		Benefit-risk ratio (prevented:induced)	
			(per 100,000)	(per 100,000)	(95% UL)		(95% UL)
MISCAN	50-80 yrs	3.5	3580	150	(80-280)	24:1	(13:1-45:1)
	40-80 yrs	4.5	3740	230	(110-410)	16:1	(9:1-34:1)
	65-80 yrs	2.0	2700	60	(30-100)	45:1	(27:1-90:1)
	50-64 yrs*	2.3	880	120	(70-220)	7:1	(4:1-13:1)
	40-49 yrs**	1.8	160	110	(50-210)	1.5:1	(0.8:1-3:1)
CRC-SPIN	50-80 yrs	3.5	4780	150	(80-280)	32:1	(17:1-60:1)
	40-80 yrs	4.5	5000	230	(110-410)	22:1	(12:1-45:1)
	65-80 yrs	2.0	4010	60	(30-100)	67:1	(40:1-134:1)
	50-64 yrs*	2.3	770	120	(70-220)	6:1	(4:1-11:1)
	40-49 yrs**	1.8	220	110	(50-210)	2:1	(1:1-4:1)
SimCRC	50-80 yrs	3.5	5190	150	(80-280)	35:1	(19:1-65:1)
	40-80 yrs	4.5	5680	230	(110-410)	25:1	(14:1-52:1)
	65-80 yrs	2.0	3390	60	(30-100)	57:1	(34:1-113:1)
	50-64 yrs*	2.3	1800	120	(70-220)	15:1	(8:1-26:1)
	40-49 yrs**	1.8	490	110	(50-210)	4:1	(2:1-10:1)

Radiation risks from screening 40-49, 50-64 and 65-80 do not equal the sum of the risks from screening 40-80 or 50-80 because the total number of CT colonography screens performed differs. UL – uncertainty limits.

*Additional benefit/risk from CT colonography screening age 50-64, assuming screening continues age 65-80.

**Additional benefit/risk from CT colonography screening age 40-49, assuming screening continues age 50-80.

Table 3

Comparison of the estimated number of radiation-related cancer deaths with the number of colorectal cancer deaths prevented by CT colonography screening every five years (per 100,000): according to microsimulation model and age at screening

Microsimulation model	Age at screening	Average no. of screens (per person)	Colorectal cancer deaths prevented	Radiation-induced cancer deaths		Benefit-risk ratio (prevented:induced)	
			(per 100,000)	(per 100,000)	(95% UL)		(95% UL)
MISCAN	50-80 yrs	3.5	2080	60	(30-110)	35:1	(19:1-69:1)
	40-80 yrs	4.5	2150	90	(40-150)	24:1	(14:1-54:1)
	65-80 yrs	2.0	1620	20	(10-50)	81:1	(32:1-162:1)
	50-64 yrs*	2.3	460	40	(30-80)	11:1	(6:1-15:1)
	40-49 yrs**	1.8	70	40	(20-80)	2:1	(0.9:1-4:1)
CRC-SPIN	50-80 yrs	3.5	2370	60	(30-110)	40:1	(22:1-79:1)
	40-80 yrs	4.5	2500	90	(40-150)	28:1	(17:1-63:1)
	65-80 yrs	2.0	1740	20	(10-50)	87:1	(35:1-174:1)
	50-64 yrs*	2.3	630	40	(30-80)	16:1	(8:1-21:1)
	40-49 yrs**	1.8	130	40	(20-80)	3:1	(2:1-7:1)
SimCRC	50-80 yrs	3.5	2790	60	(30-110)	47:1	(25:1-93:1)
	40-80 yrs	4.5	3030	90	(40-150)	34:1	(20:1-76:1)
	65-80 yrs	2.0	1820	20	(10-50)	91:1	(36:1-182:1)
	50-64 yrs*	2.3	970	40	(30-80)	24:1	(12:1-32:1)
	40-49 yrs**	1.8	240	40	(20-80)	6:1	(3:1-12:1)

Radiation risks from screening 40-49, 50-64 and 65-80 do not equal the sum of the risks from screening 40-80 or 50-80 because the total number of CT colonography screens performed is different. UL – uncertainty limits.

*Additional benefit/risk from CT colonography screening age 50-64, assuming screening continues age 65-80.

**Additional benefit/risk from CT colonography screening age 40-49, assuming screening continues age 50-80.

Table 4

Estimated number of additional CT scans conducted to follow-up extracolonic findings* and the potential risk of radiation-related cancer incidence from these CT scans following a single screen at age 50: according to follow-up scan type (per 100,000 screened)

Screening study (reference)	Abdomen/pelvis CT		Chest CT		Whole body CT		Total	
	N scans (per 100,000)	N cancers (per 100,000)	N scans (per 100,000)	N cancers (per 100,000)	N scans (per 100,000)	N cancers (per 100,000)	N scans (per 100,000)	N cancers (per 100,000)
Gluecker (2003)	2500	2	10000	5	0	0	12500	7
Pickhardt (2008)	2300	2	300	0.2	300	0.3	2900	2.5
Yee (2005)	2800	3	600	0.3	0	0	3400	3.3

*Based on the frequency of follow-up scans in the three screening studies in the table (16-18).

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