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Radiation-Induced Breast Cancer Incidence and Mortality from Digital Mammography Screening: A Modeling Study

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Abstract

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Background—Estimates of radiation-induced breast cancer risk from mammography screening have not previously considered dose exposure variation or diagnostic work-up after abnormal screening.

Objective—To estimate distributions of radiation-induced breast cancer incidence and mortality from digital mammography screening, considering exposure from screening and diagnostic mammography and dose variation across women.

Design—Two simulation-modeling approaches using common data on screening mammography from the Breast Cancer Surveillance Consortium and radiation dose from mammography from the Digital Mammographic Imaging Screening Trial.

Setting—U.S. population.

Patients—Women aged 40–74 years.

Interventions—Annual or biennial digital mammography screening from age 40, 45, or 50 until 74.

Measurements—Lifetime breast cancer deaths averted (benefits) and radiation-induced breast cancer incidence and mortality per 100,000 women screened (harms).

Results—On average, annual screening of 100,000 women aged 40 to 74 years was projected to induce 125 breast cancers (95% confidence interval [CI]=88–178) leading to 16 deaths (95% CI=11–23) relative to 968 breast cancer deaths averted by early detection from screening. Women exposed at the 95th percentile were projected to develop 246 radiation-induced breast cancers leading to 32 deaths per 100,000 women. Women with large breasts requiring extra views for complete breast examination (8% of population) were projected to have higher radiation-induced breast cancer incidence and mortality (266 cancers, 35 deaths per 100,000 women), compared to women with small or average breasts (113 cancers, 15 deaths per 100,000 women). Biennial screening starting at age 50 reduced risk of radiation-induced cancers 5-fold.

Limitations—We were unable to estimate years of life lost from radiation-induced breast cancer.

Conclusions—Radiation-induced breast cancer incidence and mortality from digital mammography screening are impacted by dose variability from screening and resultant diagnostic work-up, initiation age, and screening frequency. Women with large breasts may be at higher risk of radiation-induced breast cancer; however, the benefits of screening outweigh these risks.

INTRODUCTION

Exposure to ionizing radiation from repeated mammography examinations may increase breast cancer risk (1, 2). Radiation-induced breast cancer incidence and mortality associated with recommended screening strategies is suggested to be low relative to breast cancer deaths prevented (3–5); however, prior projected population risks were based on exposure from screening only and assumed only four standard views per screen at the mean radiation dose. Evaluations of screening programs should consider full episodes of care including diagnostic work-up prompted by an abnormal screening examination (6). False-positive recalls, breast biopsies, and short-interval follow-up examinations are relatively common in the United States and add radiation exposure from diagnostic mammography (7). Some subgroups of women, such as obese women and women with dense breast tissue, are more likely to undergo additional evaluations (7–9), increasing their risk of radiation-induced cancer.

When evaluating radiation-induced breast cancer risk, it may also be important to consider variation in radiation dose from a single examination. Exams vary in the number of views performed and dose per view, leading some women to receive more than the mean radiation dose. The American College of Radiology Imaging Network (ACRIN) Digital Mammographic Imaging Screening Trial (DMIST) found an average radiation dose to the breast of 1.86 mGy from a single digital mammography screening view (10), but dose per view varied widely from 0.15 to 13.4 mGy (Supplemental Content) and 21% of digital screening examinations used more than four views (10). Radiation dose is strongly correlated with compressed breast thickness; thus, large-breasted women tend to receive higher doses per view and may require more than four views for complete examination (10, 11). Women with breast augmentation receive implant-displacement views in addition to standard screening views, doubling their screening radiation dose (12). Any woman may undergo repeat views because of movement artifacts or improper breast positioning.

We estimated the distribution of cumulative radiation dose and associated breast cancer risk from full screening episodes to identify subgroups of women who may be at higher risk of radiation-induced cancers because they have factors associated with higher doses per exam or frequent false-positive screening examinations resulting in additional radiation exposure from subsequent diagnostic work-up. Using population-based data from the Breast Cancer Surveillance Consortium (BCSC) (13), we estimated the probability of having a false-positive screening mammogram followed by additional imaging evaluation, short-interval follow-up, and/or biopsy. We used BCSC data and information from DMIST and other sources in two simulation models to estimate radiation exposure and radiation-induced breast cancer incidence and mortality associated with eight potential screenings strategies with different start ages (40, 45, or 50 years) and screening intervals (annual, biennial, or a hybrid strategy).

METHODS

Screening Strategies

We used two complementary stochastic modeling approaches to evaluate eight strategies for screening with digital mammography:

1. Annual screening from ages 40–74, 45–74, and 50–74 years.
2. Biennial screening from ages 40–74, 45–74, and 50–74 years.
3. Hybrid strategy of annual screening from ages 40–49 or 45–49 and biennial screening from ages 50–74 years.

We included the hybrid strategies because more frequent screening has been advocated for younger and premenopausal women because they have a higher prevalence of dense breasts and more aggressive tumors, resulting in a higher risk of interval cancer, compared to older women (14–17). Outcomes include breast cancer deaths averted (benefits) and radiation-induced breast cancer incidence and mortality (harms) associated with a lifetime of mammography screening relative to no screening.

Simulation Modeling Approaches

Figure 1 summarizes our approach. We used two complementary stochastic modeling approaches to simulate mammography events associated with radiation exposure and outcomes for a population compliant with each of the eight screening strategies. The first approach used the MISCAN-Fadia microsimulation model (18), which is a detailed breast cancer natural history model. This approach provided estimates of breast cancer incidence and mortality with and without screening to contextualize estimates of radiation-induced breast cancers. Although MISCAN-Fadia models the (average) effects of screening on a population level, it does not model correlation among repeated mammography results within individual women or the specific types of work-up following an abnormal screen; therefore, it cannot be used to estimate the distribution of cumulative radiation exposure from both screening mammography and subsequent diagnostic work-up across women. Therefore, we developed a new simulation model that provides woman-level radiation exposure histories not available from the MISCAN-Fadia model. This new model captures exposure heterogeneity by simulating mammography results and subsequent workup in each woman, as well as allowing for variability in radiation exposure across women and due to breast size.

MISCAN-Fadia Simulation Model

The MISCAN-Fadia microsimulation model simulates individual life histories of women with and without breast cancer in the presence and absence of screening from birth to death from breast cancer or other causes. The model has been described in detail elsewhere (18) and information about the model can be found online (http://cisnet.cancer.gov/); inputs and assumptions are described in our report for the draft USPSTF recommendations (19). Briefly, based on BCSC data on digital mammography screening sensitivity, cancer detection rates, and cancer stage at detection, we estimated thresholds at which tumors become screen detectable. Screening sensitivity and specificity depended on age, breast density, and screening interval; breast cancer risk depended on age and breast density. The impact of screening on breast cancer natural history was assessed by modeling continuous tumor growth, where tumors detected before their fatal diameter were cured and tumors detected past their fatal diameter led to breast cancer death. We assumed that all women received the mean dose per screening exam and, if recalled, the mean dose associated with diagnostic work-up after false-positive screening, both estimated from the radiation exposure model. We also projected breast cancer incidence and mortality with and without screening.

Radiation Exposure Simulation Model

Full details including approach, data sources, and assumptions are available in the Supplemental Content. Briefly, for each of the eight screening strategies, we simulated woman-level factors and screening-related events for 100,000 women.

Woman-level factors—Each woman was assigned a compressed breast thickness from the DMIST distribution (Supplemental Table 2). Women with a compressed breast thickness of 7.5 cm or larger (8% of DMIST population) were assumed to have large breasts requiring extra views for complete examination. Based on distributions observed in the BCSC, each woman was assigned a baseline Breast Imaging-Reporting and Data System (BI-RADS) (12) density at the start of screening, which could potentially decrease by one category at ages 50 and 65 years (20) (Supplemental Table 4).

Evaluation of a positive screening exam—For each screening strategy, we simulated events following a positive screening exam that did not result in a breast cancer diagnosis (Figure 2) to focus on risk of first breast cancers induced by radiation. The probability of each event was modeled using data from digital mammograms performed at BCSC facilities from 2003–2011 on women aged 40–74 without a history of breast cancer or cancer diagnosed within 1 year after the exam. At each screening mammogram, a woman's probability of recall for additional imaging was based on her age, breast density, screening interval, and prior screening mammogram results. If recalled, the probability of referral to biopsy, short interval follow-up, or return to routine screening was based on her age, breast density, and screening interval.

Radiation dose—For each screening and diagnostic event, we sampled the number of screening mammography views from the DMIST distribution (Supplemental Table 1) and number of views for diagnostic work-up based on expert opinion, conditional on compressed breast thickness (Supplemental Table 3). We assumed different distributions of views for women with and without large breasts. We randomly sampled the radiation dose per view based on the DMIST distribution conditional on the woman's compressed breast thickness (Supplemental Figure 1). For each age, we calculated total breast-level dose by multiplying half the number of views on both breasts with the dose per view. We report the mean and the 5^{th}, 25^{th}, 75^{th}, and 95^{th} percentiles (to quantify exposure leading to increased risk of a radiation-induced cancer) for the number of mammography views and associated dose from each screening exam and all follow-up mammography within 1 year of a screen in Supplemental Table 9.

Radiation-induced breast cancer incidence and mortality

Radiation-induced breast cancer incidence was estimated using the excess absolute risk model from pooled analysis of four cohorts by Preston et al. (1), the preferred model for estimating radiation-induced breast cancer incidence (2, 21). Details are provided in the Supplemental Content. Women in these cohorts were exposed to cumulative radiation doses to the breast of 20 mGy and higher. This level of cumulative radiation exposure is reached after two to four years of mammography screening and diagnostic work-up (Supplemental Table 9). This model assumes that excess risk of radiation-induced breast cancer increases linearly with increasing radiation dose within the exposure ranges from mammography. In addition, risk decreases with increasing age at exposure, especially after age 50 (a surrogate for menopause) and increases with attained age, with the highest incidence of radiation-induced breast cancer late in life. We modeled the latency period for developing radiation-induced breast cancer using a logistic function that phases in increased breast cancer risk between 4 and 11 years after exposure (21). Radiation-induced breast cancer mortality was estimated by multiplying radiation-induced breast cancer incidence by the age-specific case-fatality rates derived from MISCAN-Fadia assuming 100% adherence to screening and current treatment. We assumed that breast cancers induced by radiation are screen detected at the same rate as non-induced cancers. Confidence Intervals (CI) were approximated by re-estimating risk using the upper and lower 95% CIs for the risk coefficient, β, given this uncertainty dominates the uncertainty in estimated risk (2, 21).

The MISCAN-Fadia model is programmed in Delphi. All other analyses were performed in R, version 3.1.0 (R Foundation for Statistical Computing) and SAS version 9.4 (SAS Institute, Cary, NC).

Role of the funding source

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RESULTS

Radiation exposure

The majority of radiation exposure from screening and subsequent diagnostic work-up was due to the screening examination (Supplemental Table 9). Diagnostic work-up accounted for only 10% of the mean annual radiation dose but 24% of the dose for women with exposure at the 95th percentile. Women with large breasts were exposed to 1.8 times higher radiation dose, on average, than women without large breasts.

Radiation-induced breast cancer incidence and breast cancer death

Risk estimates corresponding to mean exposures were similar for the two modeling approaches (Table 1), so we focus on results from the radiation exposure model. We projected that annual screening and diagnostic work-up of 100,000 women aged 40 to 74 (35 screening examinations per woman), would induce, on average, 125 breast cancers (95% CI=88–178) resulting in 16 deaths (95% CI=11–23) (Table 1). Risk projections varied widely across women, with 100,000 women exposed at the 5th percentile projected to develop 64 radiation-induced cancers (95% CI=44–90) resulting in 8 deaths (95% CI=6–12) and women exposed at the 95th percentile projected to develop 246 radiation-induced cancers (95% CI=171–349) resulting in 32 deaths (95% CI=22–45). Women with large breasts requiring extra views for complete examination were at higher risk, with more than twice as many radiation-induced breast cancers (mean=266, 95% CI=186–380) and breast cancer deaths (mean=35, 95% CI=24–50) compared to women with small or average breasts (113 breast cancers [95% CI=79–161]; 15 breast cancer deaths [95% CI=10–21]) (Table 2).

Starting screening at age 50 and following a biennial strategy (13 screening mammograms) greatly reduced risk of radiation-induced cancer and cancer death (Table 1). Compared to annual screening from 40–74 years, biennial screening from 50–74 was projected to result in one-fifth as many radiation-induced breast cancers (mean 125 [95% CI =88–178] vs. 27 [95% CI =19–38] per 100,000 women, respectively and 266 [95% CI =186–380] vs. 57 [95% CI =40–82] per 100,000 women with large breasts) (Table 2).

Breast cancer deaths averted per radiation-induced cancer

From the MISCAN-Fadia model, we projected that 16,947 breast cancers would be diagnosed from age 40 through death per 100,000 women screened annually from age 40–74 (data not shown). The number of breast cancer deaths averted ranged from 627 per 100,000 women screened biennially from age 50–74 to 968 per 100,000 women screened annually from 40–74 (Table 3). For biennial screening from age 50–74, we projected a mean of 23 breast cancer deaths averted for each radiation-induced breast cancer (95% CI =16–33; 5th percentile=48; 95th percentile=11) and 140 breast cancer deaths averted for each radiation-induced breast cancer death (95% CI =98–199; 5th percentile=289; 95th percentile=68). For annual screening from age 40–74, these ratios were lower at 8 breast cancer deaths averted per radiation-induced cancer (95% CI =5–11; 5th percentile=15; 95th percentile=4) and 59 breast cancer deaths averted per radiation-induced death among all women (95% CI =42–85; 5th percentile=117; 95th percentile=30). For annual screening from age 40–74 of women with large breasts, these ratios were even lower at 4 breast cancer deaths averted per radiation-induced cancer (95% CI =3–5) and 28 per radiation-induced death (95% CI =20–40).

DISCUSSION

We improved on previous estimates of the potential harms from radiation exposure of breast cancer screening strategies by using methods that more fully represent the experience of women who undergo routine digital screening mammography. Our models included radiation exposure from diagnostic evaluations prompted by abnormal screening examinations and incorporated variation in dose at each screening and diagnostic examination. In addition to the mean, we reported the 5th and 95th percentile of the population distribution to highlight that some women are at substantially lower- or higher-than-average risk because of variation in radiation exposure across women. The majority of the increased risk was due to screening examinations with more than four views and higher-than-average doses per view. We used DMIST data to model the number of views per screening examination and to incorporate the increased radiation dose per view for thicker compressed breasts. However, even for a given compressed breast thickness, some women received higher doses than others, likely due to higher breast density requiring more radiation to penetrate the breast. Given women with large breasts may require more views per exam and tend to receive a higher dose per view, breast size was an important factor in determining radiation exposure and associated breast cancer risk. Another reason for higher radiation exposure is false-positive exams, which accounted for 1/4th the dose received by women at the 95th percentile compared to only 1/10th the dose received by women at the mean.

Relative to a projected 16,947 breast cancers diagnosed per 100,000 women age 40 and older under annual screening, we estimate that the number of breast cancers induced by screening is likely to be very small, even for women with the highest exposures. However, relative to the number of breast cancer deaths averted with screening, radiation-induced breast cancer incidence is not trivial. Most concerning are numbers projected for annual screening and screening before age 50 of women with large breasts requiring extra views for complete breast examination, who are at more than twice the risk of radiation-induced breast cancer as women with small or average breasts. Although we did not model this explicitly, women with breast augmentation should have also have double the radiation-induced breast cancer risk, because they receive implant displacement views in addition to standard screening views, resulting in a minimum of eight views per screening exam compared to the standard four views (12).

The benefit-harm ratio in terms of terms of breast cancer deaths averted per radiation-induced breast cancer could be improved by initiating screening at age 50 instead of 40, thereby reducing risk of radiation-induced breast cancers by 60%, or by biennial screening, which would cut the risk in half compared with annual screening. Doing both – screening biennially from age 50–74 years – would reduce the risk almost five-fold compared with annual screening from age 40–74 years. To further improve the benefit-harm ratio, several steps should be taken. Current efforts to reduce the radiation dose per view should continue. Radiology staff should strive to minimize the number of additional views performed and to lower false-positive rates, which are much higher in the US than many other countries, suggesting room for improvement (22–25). Radiation doses from diagnostic mammography could be avoided for certain screen-detected masses amenable to ultrasound work-up alone. In addition, facilities should ensure that women with large breasts are imaged using larger detector sizes, to minimize the need for extra views for complete breast examination.

Hendrick (3) also estimated radiation-induced breast cancer incidence and mortality using DMIST dose data, but used the mean dose for four views without accounting for the 21% of women who received more than four views or follow-up imaging. He projected that annual screening of 100,000 women from age 40–80 with an exam-level dose of 3.7 mGy would induce 72 breast cancers leading to 20 deaths. For women screened annually from age 40–74, we estimated fewer breast cancer deaths (16/100,000) despite more radiation-induced breast cancers (125/100,000) because we optimistically assumed 100% adherence to the screening regimen and use of currently available breast cancer treatments. Specifically, we assumed 10–19% of women diagnosed with breast cancer between ages 40–74 would die of the disease (depending on screening scenario) compared to recent estimates of more than 23% (26). Thus, we may have underestimated the number of radiation-induced breast cancer deaths. Yaffe and Mainprize (4) projected that screening 100,000 women annually from age 40–55 years and biennially thereafter to age 74 years with a dose of 3.7 mGy would induce 86 breast cancers and 11 breast cancer deaths. In comparison, we projected that screening 100,000 women annually from 40–49 years and biennially thereafter to age 74 years would induce 89 breast cancers and 15 breast cancer deaths. Our estimates are likely higher because we accounted for some screening examinations having more than four views and for radiation exposure from diagnostic work-up.

Doses from current digital mammography systems may be lower than doses from older DMIST units. Nevertheless, DMIST doses may still be conservative because, like most prior studies, dose estimates assumed breast compositions of 50% glandular tissue, which likely underestimates dose by 8–18% (27, 28). Although Mammography Quality Standards Act inspections suggest that doses for a digital mammography view decreased 2.5% between 2007 and 2009 (29), these doses were measured with phantoms simulating breasts with a compressed breast thickness at the 30th percentile in DMIST. Radiation dose is highly correlated with compressed breast thickness, which may be increasing over time with increasing population body mass index (BMI) (30).

The use of digital breast tomosynthesis for screening is increasing in the United States (31). Doses from breast tomosynthesis vary by the strategy used; however, in general, the three-dimensional tomosynthesis acquisition results in a radiation dose similar to or slightly higher than standard digital mammography (28, 32, 33). Currently, most US practices offering screening tomosynthesis combine tomosynthesis with digital mammography, effectively doubling doses, which doubles the radiation-induced cancer risk. FDA-approved software that generates synthetic two-dimensional views from tomosynthesis acquisitions is likely to eliminate the need for standard digital mammography views and their associated radiation exposure (34); however, it is unknown how quickly this software will diffuse into clinical practice. Estimating radiation-induced cancer risks associated with tomosynthesis screening is further complicated by the expectation that tomosynthesis will decrease recall rates and potentially eliminate the need for diagnostic mammography to work-up some imaging findings (35–41).

Our study had several limitations. We had limited information on the percentage of women requiring more than four views for complete breast examination. In DMIST, 21% of women required more than four views (10), although most received only one or two extra views, likely due to patient movement or poor positioning. Based on the observed distribution of compressed breast thickness and number of views, we assumed 8% of women received extra views due to large breasts. Importantly, the early-generation mammography systems used in DMIST had smaller image detectors (10). Most modern units have larger detectors, so the percentage of women requiring extra views due to large breast size is likely less than 8%.

We were unable to calculate the years of life lost due to radiation-induced breast cancers, which may occur later in life than deaths prevented from screening. Due to lack of data, we did not model the association between breast size and the probability of a false-positive mammogram; thus, we may have underestimated exposure from additional work-up in women with large breasts given obese women are 20% more likely than normal-weight women to have false-positive mammograms (9). Also, we assumed the number of breast cancer deaths averted with screening did not vary by breast size; however, screening may prevent a larger number of deaths among postmenopausal obese women (who tend to have large breasts) given they are at higher risk of advanced disease (42). We also did not model the association between breast density and radiation dose per view due to lack of representative data. Probabilities for events following screening mammograms were based on point estimates from models that used the best available data, and did not account for uncertainty due to model misspecification or inherent variability in parameter estimates. We were unable to estimate 95% confidence intervals for deaths averted with screening due to the computational complexity of the MISCAN-Fadia model and because many input parameters of the model (such as tumor growth rate) are unobservable and therefore, have unknown distributions. Last, we made several simplifying assumptions (discussed in the supplement).

In conclusion, population projections of radiation-induced breast cancer incidence and mortality from mammography screening are affected by variability in doses from screening and resultant diagnostic examinations, age at screening initiation, and screening frequency. Our study suggests that women with large breasts or breast augmentation receive higher radiation doses and may be at higher risk of a radiation-induced breast cancer and breast cancer death. Radiology practices should strive to ensure that women with large breasts undergo screening mammography using large image detectors with the fewest number of views possible.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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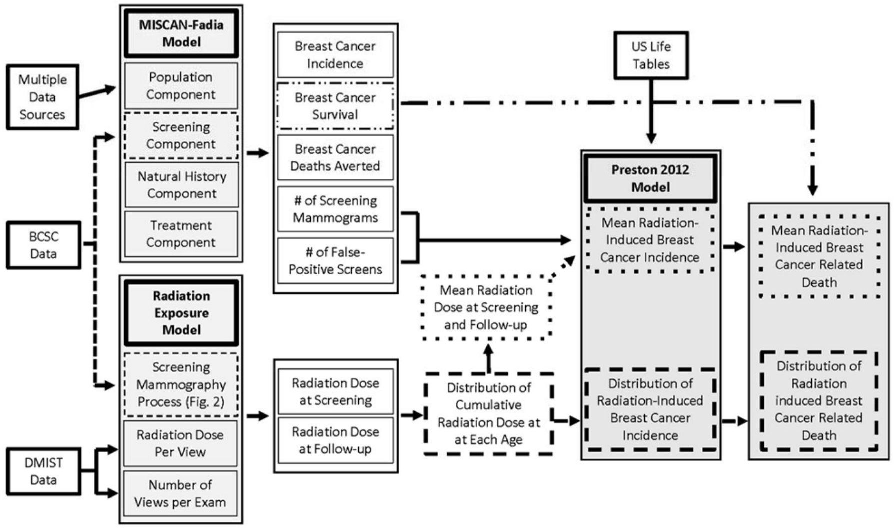

Figure 1.

Schematic of two modeling approaches used to simulate mammography events and outcomes associated with the eight screening strategies. Estimates of the number of screening exams and false-positive screens from the MISCAN-Fadia model were combined with the mean radiation dose from the Radiation Exposure Model to estimate *mean* radiation-induced breast cancer incidence. Estimates of the distribution of cumulative radiation dose at each age across women from the Radiation Exposure Model were used to estimate the *distribution* of radiation-induced breast cancer incidence. Radiation-induced breast cancer incidence was combined with breast cancer survival estimates from the MISCAN-Fadia model to estimate radiation-induced breast cancer mortality.

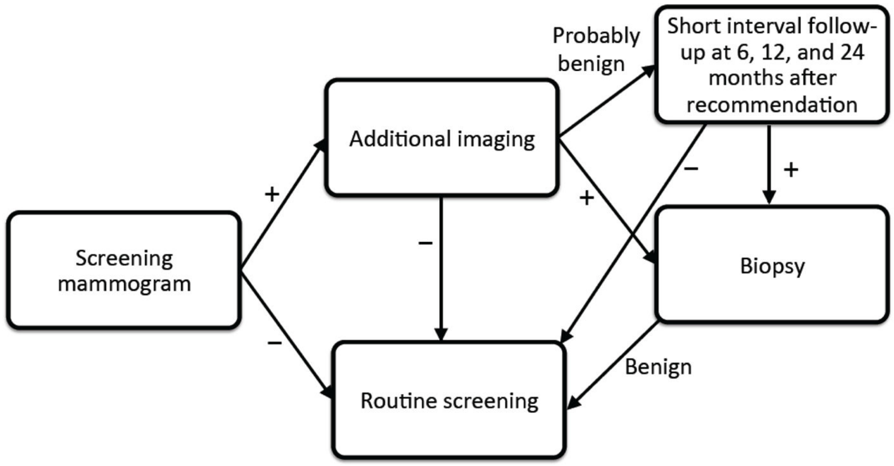

Figure 2.
Screening mammography process. Short interval follow-up (SIFU) examinations included unilateral, diagnostic views on the recalled breast at 6 months after the initial SIFU recommendation, and both unilateral, diagnostic views on the recalled breast plus bilateral routine screening views at 12 and 24 months after the initial SIFU recommendation for annual screeners and 24 months after the initial SIFU recommendation for biennial screeners. The routine screening views could result in recall for additional imaging to work up a new finding, followed by a recommendation for another SIFU examination, or tissue biopsy.

Table 1

Comparison of lifetime attributable risks of radiation-induced breast cancer and breast cancer death (per 100,000 women) from two modeling approaches.

	MISCAN-Fadia Model		Radiation-Exposure Model	
Screening Strategy	**Mean (95% CI)**	**Mean (95% CI)**	**5th percentile (95% CI)**	**95th percentile (95% CI)**
	Lifetime Attributable Risk of Radiation-Induced Breast Cancer (Per 100,000 Women)			
Biennial screening				
Ages 50–74 y	28 (20, 40)	27 (19, 38)	13 (9, 19)	55 (39, 78)
Ages 45–74 y	44 (31, 62)	45 (31, 64)	21 (15, 30)	92 (65, 130)
Ages 40–74 y	67 (47, 96)	68 (48, 97)	33 (23, 47)	138 (97, 196)
Hybrid strategy				
A45–49 y, B50–74 y	57 (40, 81)	59 (41, 84)	29 (20, 41)	118 (82, 168)
A40–49 y, B50–74 y	101 (71, 143)	89 (62, 126)	44 (31, 62)	177 (125, 251)
Annual screening				
Ages 50–74 y	54 (39, 75)	49 (34, 69)	25 (17, 35)	97 (68, 139)
Ages 45–74 y	85 (59, 121)	81 (57, 115)	41 (29, 58)	159 (111, 226)
Ages 40–74 y	129 (90, 183)	125 (88, 178)	64 (44, 90)	246 (171, 349)
	Lifetime Attributable Risk of Radiation-Induced Breast Cancer Death (Per 100,000 Women)			
Biennial screening				
Ages 50–74 y	5 (3, 7)	4 (3, 6)	2 (2, 3)	9 (6, 13)
Ages 45–74 y	8 (5, 11)	8 (5, 11)	4 (3, 5)	16 (11, 22)
Ages 40–74 y	12 (8, 17)	12 (8, 17)	6 (4, 8)	24 (17, 34)
Hybrid strategy				
A45–49 y, B50–74 y	10 (7, 14)	10 (7, 14)	5 (3, 7)	20 (14, 29)
A40–49 y, B50–74 y	18 (13, 25)	15 (11, 22)	8 (5, 11)	31 (22, 44)
Annual screening				
Ages 50–74 y	7 (5, 10)	7 (5, 9)	3 (2, 5)	13 (9, 19)
Ages 45–74 y	11 (8, 16)	11 (8, 15)	5 (4, 8)	21 (15, 30)
Ages 40–74 y	16 (12, 23)	16 (11, 23)	8 (6, 12)	32 (22, 45)

CI, confidence interval; y, years; A, annual screening at ages 40–50 or 45–50 and B, biennial screening at 50–74 years.

Table 2

Mean, 5th percentile, and 95th percentile (95% confidence intervals) of lifetime attributable risks (per 100,000 women) of radiation-induced breast cancer and breast cancer death, by breast size, for different screening strategies.

	Small or average breasts			Large breasts		
Screening Strategy	**Mean (95% CI)**	**5th percentile (95% CI)**	**95th percentile (95% CI)**	**Mean (95% CI)**	**5th percentile (95% CI)**	**95th percentile (95% CI)**
Lifetime Attributable Risk of Radiation-Induced Breast Cancer (Per 100,000 Women)						
Biennial screening						
Ages 50–74 y	24 (17, 35)	13 (9, 18)	43 (30, 61)	57 (40, 82)	28 (19, 40)	108 (77, 154)
Ages 45–74 y	40 (28, 57)	21 (15, 30)	72 (50, 102)	95 (67, 135)	46 (32, 65)	181 (128, 259)
Ages 40–74 y	61 (43, 87)	33 (23, 46)	107 (76, 152)	144 (100, 205)	71 (49, 101)	266 (188, 384)
Hybrid strategy						
A45–49 y, B50–74 y	53 (37, 75)	29 (20, 41)	91 (64, 130)	125 (87, 178)	60 (43, 88)	233 (162, 335)
A40–49 y, B50–74 y	80 (56, 114)	43 (31, 62)	137 (96, 195)	189 (132, 269)	95 (65, 134)	351 (244, 495)
Annual screening						
Ages 50–74 y	44 (31, 62)	25 (17, 35)	74 (52, 105)	104 (73, 149)	53 (37, 76)	187 (131, 267)
Ages 45–74 y	73 (51, 103)	40 (28, 57)	122 (85, 174)	173 (121, 245)	88 (62, 126)	315 (221, 445)
Ages 40–74 y	113 (79, 161)	63 (44, 89)	189 (133, 268)	266 (186, 380)	136 (95, 193)	487 (339, 700)
Lifetime Attributable Risk of Radiation-Induced Breast Cancer Death (Per 100,000 Women)						
Biennial screening						
Ages 50–74 y	4 (3, 6)	2 (1, 3)	7 (5, 10)	10 (7, 14)	5 (3, 7)	18 (13, 26)
Ages 45–74 y	7 (5, 10)	4 (3, 5)	12 (9, 17)	16 (11, 23)	8 (5, 11)	31 (22, 44)
Ages 40–74 y	11 (7, 15)	6 (4, 8)	19 (13, 26)	25 (17, 35)	12 (8, 17)	46 (33, 67)
Hybrid strategy						
A45–49 y, B50–74 y	9 (6, 13)	5 (3, 7)	16 (11, 22)	21 (15, 31)	10 (7, 15)	40 (28, 57)
A40–49 y, B50–74 y	14 (10, 20)	8 (5, 11)	24 (17, 34)	33 (23, 47)	16 (11, 23)	61 (42, 86)
Annual screening						
Ages 50–74 y	6 (4, 9)	3 (2, 5)	10 (7, 14)	14 (10, 20)	7 (5, 10)	25 (18, 36)
Ages 45–74 y	10 (7, 14)	5 (4, 8)	16 (11, 23)	23 (16, 33)	12 (8, 17)	42 (29, 59)
Ages 40–74 y	15 (10, 21)	8 (6, 12)	25 (17, 35)	35 (24, 50)	18 (12, 25)	63 (44, 91)

CI, confidence interval; y, years; A, annual screening at ages 40–50 or 45–50 and B, biennial screening at 50–74 years.

Table 3

Number of breast cancer deaths averted by screening 100,000 women and ratio of number of breast cancer deaths averted per number (mean, 5th percentile, and 95th percentile) of radiation-induced breast cancers and of radiation-induced breast cancer deaths.

Strategy	Number of breast cancer deaths averted by screening	Overall			Small or average breasts	Large breasts
		Mean (95% CI)	5th Percentile (95% CI)	95th Percentile (95% CI)	Mean (95% CI)	Mean (95% CI)
		Ratio of Breast Cancer Deaths Averted per Radiation-Induced Breast Cancer				
Biennial screening						
Ages 50–74 y	627	23 (16, 33)	48 (34, 69)	11 (8, 16)	26 (18, 37)	11 (8, 16)
Ages 45–74 y	666	15 (10, 21)	31 (22, 45)	7 (5, 10)	17 (12, 24)	7 (5, 10)
Ages 40–74 y	732	11 (8, 15)	22 (16, 32)	5 (4, 8)	12 (8, 17)	5 (4, 7)
Hybrid strategy						
A45–49 y, B50–74 y	717	12 (9, 17)	25 (17, 35)	6 (4, 9)	14 (10, 19)	6 (4, 8)
A40–49 y, B50–74 y	780	9 (6, 13)	18 (12, 25)	4 (3, 6)	10 (7, 14)	4 (3, 6)
Annual screening						
Ages 50–74 y	819	17 (12, 24)	33 (23, 47)	8 (6, 12)	19 (13, 27)	8 (6, 11)
Ages 45–74 y	907	11 (8, 16)	22 (16, 32)	6 (4, 8)	12 (9, 18)	5 (4, 8)
Ages 40–74 y	968	8 (5, 11)	15 (11, 22)	4 (3, 6)	9 (6, 12)	4 (3, 5)
		Ratio of Breast Cancer Deaths Averted per Radiation-Induced Breast Cancer Death				
Biennial screening						
Ages 50–74 y	627	140 (98, 199)	289 (203, 415)	68 (48, 97)	155 (109, 221)	66 (46, 93)
Ages 45–74 y	666	87 (61, 125)	184 (130, 263)	43 (30, 60)	97 (68, 139)	41 (29, 59)
Ages 40–74 y	732	62 (44, 89)	128 (90, 183)	31 (22, 44)	69 (48, 98)	29 (21, 42)
Hybrid strategy						
A45–49 y, B50–74 y	717	71 (50, 102)	145 (102, 207)	35 (25, 51)	79 (56, 113)	33 (23, 48)
A40–49 y, B50–74 y	780	51 (36, 72)	102 (72, 146)	25 (18, 36)	56 (40, 80)	24 (17, 34)
Annual screening						
Ages 50–74 y	819	123 (86, 176)	242 (171, 346)	62 (43, 89)	136 (96, 195)	58 (40, 83)
Ages 45–74 y	907	84 (60, 121)	167 (118, 239)	43 (30, 61)	94 (66, 134)	39 (28, 57)
Ages 40–74 y	968	59 (42, 85)	117 (82, 167)	30 (21, 43)	66 (46, 94)	28 (20, 40)

CI, confidence interval; y, years; A, annual screening at ages 40–50 or 45–50 and B, biennial screening at 50–74 years.