Structured Abstract

**Background:** Risk projections of radiation-induced breast cancer from mammography screening have not previously considered exposure variation or workup from abnormal screens.

**Objective:** To estimate distributions of radiation-induced breast cancer incidence and mortality under different breast cancer screening strategies, considering exposure from screening mammography and followup imaging and variation in dose.

**Materials and methods:** Using two simulation models, we estimated the distributions of radiation dose and radiation-induced breast cancer incidence and mortality associated with the screening process, including imaging following abnormal screens. We evaluated annual and biennial mammography screening from age 40, 45, or 50 years until age 74 years and hybrid strategies of annual screening starting at age 40 or 45 years and biennial screening from ages 50 to 74 years. We used population-based data from the U.S. Breast Cancer Surveillance Consortium to estimate the probability of a false-positive screening mammogram followed by diagnostic imaging evaluation, short-interval followup imaging, image-guided biopsy, and/or needle localization. We estimated cumulative radiation dose based on the distributions of the number of mammography views and dose per view from the American College of Radiology Imaging Network’s Digital Mammographic Imaging Screening Trial. Finally, we estimated radiation-induced breast cancer incidence using the Preston 2002 excess absolute risk model and mortality using the MISCAN-Fadia natural history model.

**Results:** Annual screening of women ages 40 to 74 years yielded a lifetime attributable risk (LAR) of 125 breast cancers per 100,000 women (95% confidence interval [CI], 88 to 178) and 16 deaths (95% CI, 11 to 23), with wide variability across women (95th percentile, 246 cancers [95% CI, 171 to 349] and 32 deaths [95% CI, 32 to 45] per 100,000 women), relative to 16,947 breast cancers diagnosed and 968 deaths averted by screening. Women with large breasts had higher risk of radiation-induced cancer (mean LAR, 265 cancers and 35 deaths per 100,000 women; 95th percentile, 481 cancers and 63 deaths per 100,000 women) compared to other women (mean LAR, 112 cancers and 15 deaths per 100,000 women; 95th percentile, 187 cancers and 24 deaths per 100,000 women). Biennial screening, hybrid screening, or starting at age 50 years reduced risks. For example, compared to annual screening from ages 40 to 74 years, biennial screening from ages 50 to 74 years was projected to result in an average 98 fewer breast cancers per 100,000 women screened (95th percentile, 191) and 209 fewer cancers among women with large breasts (95th percentile, 379).

**Conclusions:** On average, radiation-induced breast cancer incidence and mortality from screening are low relative to deaths averted, but they are affected by dose variability, age at initiation, and screening frequency. Women with large breasts may be at higher risk of radiation-induced breast cancer.