

Re: Lung Cancer Risk and Radiation Dose Among Women Treated for Breast Cancer

Inskip et al. (1) were able to quantify the long-term risk of lung cancer in terms of radiation dose among 897 610-year survivors of breast cancer reported to the Connecticut Tumor Registry between 1935 and 1971. The relative risk of lung cancer following treatment with adjuvant radiotherapy and radical mastectomy was approximately twofold, based on 61 case patients. Radiation fields targeted regional lymph nodes and the chest wall, resulting in large average doses to the lungs (15.2 Gy, ipsilateral lung; 4.6 Gy, contralateral lung). Lung cancer risk increased with radiation dose ($P = .18$). Radiotherapy treatments have changed in recent decades, however, employing smaller fields that result in lower radiation doses to lung (1).

We extend the analysis of secondary lung cancer risk after breast cancer utilizing data on more than 180 000 women reported to the population-based registries that comprise the Surveillance, Epidemiology, and End Results (SEER) Program¹ (1973-1991) of the National Cancer Institute (NCI). Information that is routinely provided to these registries includes the first course of cancer-directed therapy according to one of several broad designations. The extent of radiotherapy, which determines lung exposure, is not specified; however, for several sites, including breast, initial surgery is further described. Breast-conserving surgery is typically accompanied by local radiotherapy, resulting in considerably lower radiation exposure to the lung than delivered with techniques employed in the past in conjunction with more extensive resection (1). Following prior convention within the SEER Program (2), we defined breast-conserving surgery as a partial or less-than-total mastectomy. All other surgical procedures, including mastectomy, were grouped as "non-breast-conserving surgery." Because type of operation served as an imperfect surrogate for the extent of radiotherapy,

some misclassification may result. A portion of breast cancer patients reported to the SEER Program were included in a previous study (3) of secondary lung neoplasia.

Among 182 122 2-month survivors of breast cancer diagnosed between January 1, 1973, and December 31, 1991, and treated surgically, 1198 cases of lung cancer were observed (Table 1).² The risk of subsequent lung cancer increased with time to reach 1.93 (95% confidence interval [CI] = 1.48-2.47; P trend <.0001) among 5923 10-year survivors initially treated with radiotherapy and non-breast-conserving surgery. The twofold risk is in agreement with results from the Connecticut study (1). Excess risks of lung cancer among long-term survivors existed for small-cell carcinoma (observed-to-expected [O/E] ratio = 2.89; 95% CI = 1.71-4.56), squamous cell carcinoma (O/E = 2.55; 95% CI = 1.46-4.14), and adenocarcinoma (O/E = 1.62; 95% CI = 0.96-2.56). In contrast, elevated lung cancer risks were not evident among 128 534 women who were not treated with radiation.

Because breast-conserving surgery has been utilized only recently within the SEER program (average year, 1988), lung cancer risk could not be evaluated among long-term survivors. There was no increased risk, however, apparent up to about 10 years after treatment.

Our results confirm that past adjuvant radiotherapy, likely to deliver substantial doses of radiation to the lungs, is associated with a twofold risk of pulmonary neoplasia among 10-year survivors of breast cancer (1). Breast-conserving surgery and local adjuvant radiotherapy (2), which delivers lower doses to lung, might be expected to result in smaller risks of lung cancer among long-term survivors.

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Table L Risk of secondary lung cancer following adjuvant radiotherapy for breast cancer

	Time since diagnosis of breast cancer			
	2 mo to <1 y	1-4 y	5-9 y	≥10 y
No. of patients entering interval	182 122*	162 813	81 748	32 268
No. of person-years within interval	142 902	472 566	265 979	113 128

	Secondary lung cancer							
	Observed	O/E	Observed	O/E	Observed	O/E	Observed	O/E
Surgery: non-breast-conserving†								
Adjuvant radiotherapy (n = 26 201)	6	0.33‡	67	0.98	69	1.24	63	1.93‡,§
No radiotherapy (n = 128 534)	79	0.73‡	412	1.02	249	0.88‡	156	1.08
Surgery: breast-conserving 								
Adjuvant radiotherapy (n = 19 247)	18	1.10	36	0.76	10	1.02	¶	¶
No radiotherapy (n = 8140)	8	1.06	19	1.01	6	1.76	¶	¶

*Number represents 2-mo survivors of breast cancer diagnosed between January 1, 1973, and December 31, 1991, who were initially treated with surgery and reported to one of nine population-based registries participating in the SEER Program.

†Represents subcutaneous mastectomy, total mastectomy, modified radical/total mastectomy, radical mastectomy, and extended radical mastectomy.

‡P < .05.

§Trend for P < .0001.

|| Represents partial or less-than-total mastectomy (including segmental mastectomy, lumpectomy, quadrantectomy, wedge resection, nipple resection, excisional biopsy, and partial mastectomy not otherwise specified), with or without dissection of axillary lymph nodes.

¶ Given the relatively recent introduction of this surgical approach, sufficient numbers of long-term survivors are not yet available within the SEER Program to quantify the risk of secondary lung cancer.

References

- (1) Inskip PD, Stovall M, Flannery JT: Lung cancer risk and radiation dose among women treated for breast cancer. *J Natl Cancer Inst* 86:983-988, 1994
- (2) Farrow DC, Hunt WC, Samet JM: Geographic variation in the treatment of localized breast cancer [see comment citation in Medline]. *N Engl J Med* 326:1097-1101, 1992
- (3) Neugut AI, Robinson E, Lee WC, et al: Lung cancer after radiation therapy for breast cancer [see comment citation in Medline]. *Cancer* 71:3054-3057, 1993

(4) Breslow NE, Lubin JH, Marek P, et al: Multiplicative models and cohort analysis. *J Am Stat Assoc* 78:1-12, 1983

Notes

¹Editor's note: SEER is a set of geographically defined, population-based central tumor registries in the United States, operated by local nonprofit organizations under contract to the NCI. Each registry annually submits its cases to the NCI on a computer tape. These computer tapes are then edited by the NCI and made available for analysis.

²Statistical tests and 95% CIs were based on the assumption that the observed numbers of second cancers followed a Poisson distribution. Test for homogeneity and linear trend were conducted according to the methods of Breslow et al. (4). All P values were two-sided.

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