The Pattern of Breast Cancer Screening Utilization and Its Consequences

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BACKGROUND. The objective of this study was to describe the pattern of screening utilization and its consequences in terms of tumor size and time of tumor appearance of invasive breast carcinoma among a population of women who were examined at a large service screening/diagnostic program over the last decade.

METHODS. Utilization of mammography was assessed from a population of 59,899 women who received 196,891 mammograms at the Massachusetts General Hospital Breast Imaging Division from January 1, 1990 to March 1, 1999, among which 604 invasive breast tumors were found. Two hundred six invasive, clinically detected tumors also were seen during this period among women who had no record of a previous mammogram. Additional information was available on screening of women from March 1, 1999 to June 1, 2001.

RESULTS. Fifty percent of the women who used screening did not begin until the age of 50 years, although 25% of the invasive breast tumors were found in women age < 50 years. Relatively few of the women who used screening returned promptly for their annual examinations; by 1.5 years, only 50% had returned. Approximately 25% of the invasive breast tumors were found in women for whom there was no record of a previous screening mammogram, and these tumors were larger (median, 15 mm) than the screen-detected tumors (median, 10 mm). Approximately 30% of the 604 invasive breast tumors in the screening population were found on nonmammographic grounds, and they also were larger (median, 15 mm) than the screen-detected tumors (median, 10 mm). However, only 3% of these 604 tumors were found by nonmammographic criteria within 6 months of the previous negative examination, and only 12% were found within 1 year. By back calculating the likely size of each of these tumors at the time of the negative mammogram, it could be seen that most tumors probably emerged as larger, palpable masses not because they were missed at the previous negative mammogram, because most were too small then to have been detected, but because too much time had been allowed to pass.

CONCLUSIONS. Far too many women did not comply with the American Cancer Society recommendation of prompt annual screening from the age of 40 years. Consequently, almost 50% of the invasive tumors emerged as larger and, thus, potentially more lethal, palpable masses. ***Cancer* 2002;94:37–43.**

KEYWORDS: mammogram, screen detected, nonmammographic criteria, invasive tumors.

The fact that breast cancer screening saves lives has been demonstrated[1–6] by the results of randomized controlled trials. The American Cancer Society (ACS) has recommended annual screening from the age of 40 years,[6] although there is some uncertainty about the best screening frequency[7] and the age of screening initiation.[4,6] Here, we describe the pattern of screening utilization among a pop-

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TABLE 1
Invasive Breast Tumors Found in the Massachusetts General Hospital Population between January 1, 1990 and March 1, 1999 by Method of Detection and Other Characteristics[a]

Tumor type	Definition	No.	Median size (mm)	Mean size (mm)
First screen-detected tumors	Invasive breast tumors identified by mammography in asymptomatic women at their first screen at MGH	115	12	13.7
Subsequent screen-detected tumors	Invasive breast tumors identified by mammography in asymptomatic women who had at least one previous negative screening mammogram at MGH	312	10	11.7
Never-screened tumors	Invasive breast tumors identified by means other than screening mammogram in women with no history of mammography at MGH	204	15	18.7
Intervening tumors (all)	Invasive breast tumors identified by means other than screening mammogram in women who had at least one previous negative screening mammogram at MGH	179	15	16.8
Intervening tumors, within 1 year	Invasive breast tumors identified by means other than screening mammogram in women who had at least one previous negative screening mammogram at MGH and found within 1 year of the previous negative mammogram	68	14[b]	15.5[b]
Intervening tumors, after 1 year	Invasive breast tumors identified by means other than screening mammogram in women who had at least one previous negative screening mammogram at MGH and found more than 1 year after the previous negative mammogram	111	15	17.6

MGH: Massachusetts General Hospital.
[a] For further details, see Michaelson et al.[8]
[b] $P < 0.03$ for comparison of the sizes of the intervening tumors found within 1 year of the previous negative mammogram with either the intervening tumors found more than 1 year after the previous negative mammogram or with the never-screened tumors.

ulation of women at the Breast Imaging Division at the Massachusetts General Hospital (MGH) over the last decade[8] and its consequences in terms of tumor size and time of tumor appearance of invasive breast carcinoma.

MATERIALS AND METHODS

The Data Set and Basic Definitions

The utilization of mammography and the tumors seen during this period were assessed from a population of 59,899 women who received 196,891 mammograms at the MGH Breast Imaging Division from January 1, 1990 to March 1, 1999. Eight hundred ten patients with invasive breast tumors for which there was complete information on the mode of detection were seen during this period (Table 1).[8] The data base, which contained entries back to January 1, 1985, made it possible to determine which of these 810 women who had received a previous mammogram at the MGH Breast Imaging Division. Carcinomas in situ were not included. Additional information was available on screening of women from March 1, 1999 to June 1, 2001 but without information on the tumors seen.

The 810 tumors were categorized according to their method of detection into 1 of 4 categories: *never-screened tumors*, *first screen-detected tumors*, *subsequent screen-detected tumors*, and *intervening tumors* (for definitions, see below and Table 1). Of the 810 invasive breast tumors seen from January 1, 1990 to March 1, 1999, 206 were found on clinical grounds in women for whom there was no record of a previous mammogram at the MGH (never-screened tumors), although some of these women may have had a previous mammogram elsewhere. Six hundred four of 810 tumors were found in women who received a previous mammogram at the MGH. Among these 810 women, there were 427 (58%) invasive breast tumors detected by mammography (115 first screen-detected tumors [invasive breast carcinoma identified by mammography in asymptomatic women at their first screening at the MGH] and 312 subsequent screen-detected tumors [invasive breast carcinoma identified by mammography in asymptomatic women who had received a least one previous negative screening mammogram at the MGH]), whereas 383 invasive breasts tumors (42%) were identified by means other than mammography (204 never-screened tumors [invasive breast carcinoma identified by means other than a screening

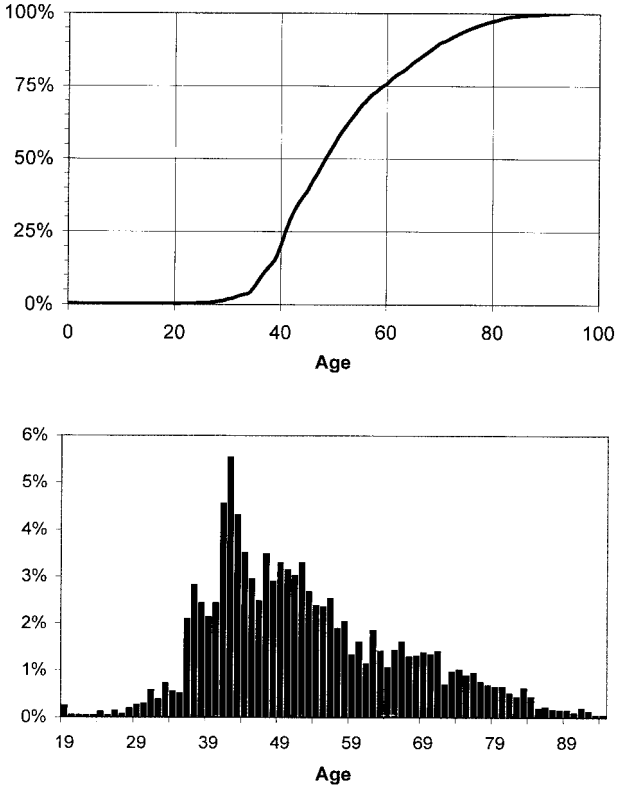

FIGURE 1. Cumulative age distribution (bottom) and age distribution (top) for women who underwent their first screening mammograms in 1998. To assess the distribution of women by age when they began screening, 1998 was chosen as a representative year; this made it possible to search the data set for the previous decade to find those women who had no record of a previous mammogram over the past decade.

mammogram in women with no history of mammography at the MGH prior to the discovery of their tumors] and 179 intervening tumors [invasive breast carcinoma identified by means other than a screening mammogram in women with at least one previous negative screening mammogram at the MGH]). We have adopted the term *intervening tumor* to distinguish it from the term *interval tumor*, which usually is used to describe a tumor arising after a negative examination but within a specified time: That is, intervening tumors can occur at any time after a negative mammogram. For the 491 tumors that arose in women with a previous negative mammogram (179 intervening tumors and 312 subsequent screen-detected tumors), we were able to determine the time between the previous negative examination and the diagnosis of the tumor. Macroscopic tumor size, measured for three dimensions, was assessed at the time of pathologic analysis, and the largest of these three measurements was entered into the MGH data base as the tumor size.

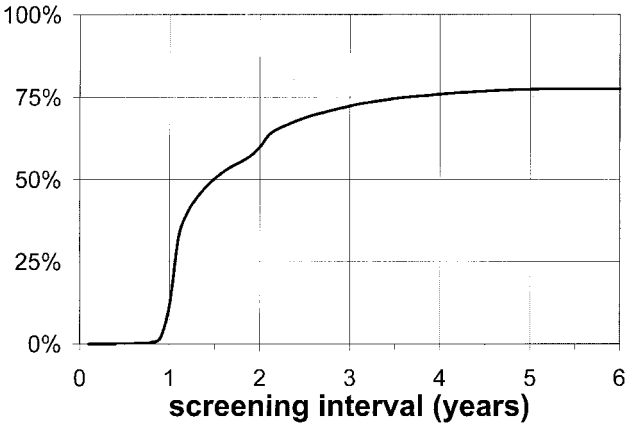

FIGURE 2. Cumulative distribution of the screening intervals, based on women who had a mammogram in 1994. Shown are the first returns from women who received a mammogram in 1994.

Three subsets of the full data set provided insight into the pattern of utilization. Four thousand ninety-five women were identified who had a mammogram in 1998 but had no record of a previous mammogram in the previous decade. We chose 1998 as a representative year, because this allowed us to search the data set to identify those women who had no record of a previous mammogram over the past decade, although some of these women may have had a previous mammogram elsewhere. From this data set, information was collected on the distribution of patients by age group (Fig. 1). There were 14,325 women who had a normal screening mammogram in 1994 who were used to estimate the pattern of screening among women at this institution, and they were studied by searching for the subsequent mammograms occurring up until May 1, 2001 (Fig. 2). Of these 14,325 women, 11,111 came in for at least one more screening mammogram, and the time until the next mammogram for each woman was identified. Three thousand two hundred fourteen of these women never came back for another mammogram at the MGH Breast Imaging Division. Finally, for 15,041 women who had mammograms in 1992, the time until they returned for subsequent mammograms up until June 1, 2001 was determined (Fig. 3). The patterns of return for the 1992 group (Fig. 2) and the 1994 group (Fig. 3) were very similar.

Estimation of Tumor Size at the Time of Screening for Tumors Found after a Previous Negative Mammogram (Intervening Tumors and Subsequent Screen-Detected Tumors)

Over the rather narrow range of sizes at which most tumors are detected, it appears likely that invasive

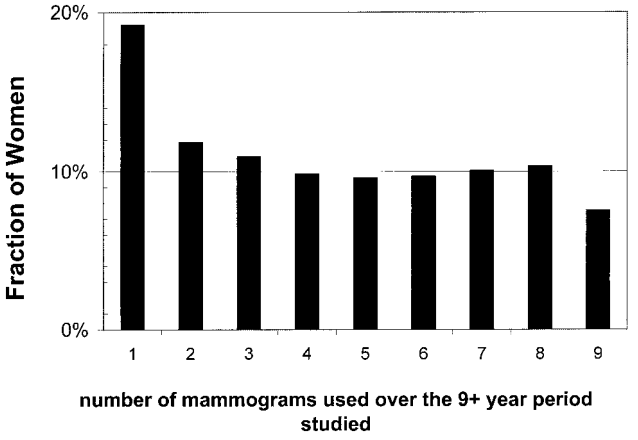

FIGURE 3. Mammography utilization during the period from January 1, 1992 to June 1, 2001 for women who had a mammogram in 1992.

breast tumor growth is exponential.[9,10] Thus, the relation between the number of cells in a tumor (N) and time (t) can be expressed as follows:

$$N = N_o e^{rt}, \quad (1)$$

where N_o is the number of cells at time $t = 0$, and e is the exponential constant, t is time. Using r is a constant,

$$r = \ln(2)/t_D, \quad (2)$$

where t_D is the tumor doubling time.

A number of studies have estimated the tumor growth rate from patients in whom the size of the tumor could be measured on two different occasions, often when the tumor could be seen on review of an earlier mammogram.[11–16] From these studies, as well as from our own data (unpublished results), it appears likely that the median breast tumor doubling time (t_D) is approximately 130 days. For those patients with tumors that were found after a negative mammogram, let us call the time since the previous negative mammogram t_p and the greatest tumor dimension at the time it was found subsequently D_f. It follows from Equation 3 that the greatest tumor dimension, (D_m) at the time the tumor was not seen at screening will be

$$D_m = D_f{*}e\hat{}((-\ln(2)/3{*}t_D){*}t_p). \quad (3)$$

RESULTS

Few of Women who Utilized Screening Began Screening at Age 40 Years, and Only Half Began by Age 50 Years

The median age for women at their first screening mammograms at MGH was 50 years (Fig. 1). Approximately 20% of women began screening by age 40 years, approximately 40% began by age 45 years, and approximately 50% began by age 50 years. This contrasts with the fact that 25% of the invasive breast tumors in this data set occurred in women age < 50 years.[8] Although some of these women may have had an earlier mammogram at another institution, the general impression seems clear that few women begin screening at age 40 years, as recommended by the ACS.

Prompt Attendance at Recommended Annual Screening Was Not Widespread

Among the women who had a previous negative mammogram, 50% had not returned for a second mammogram 1.5 years later, and approximately 40% had not returned by 2 years (Fig. 2). For almost one in five women, there was no record that they ever returned for a second examination, although some of these women may have gone elsewhere for a screening mammogram (Figs. 2, 3).

Another indication of the incomplete utilization of screening was observed in the analysis of the number of mammograms administered from January 1, 1992 to June 1, 2001 to women who had received a mammogram in 1992 (Fig. 3). Fewer than 10% of these women took advantage of all nine mammograms that would have resulted from complete compliance with the ACS recommendation of annual screening, whereas more than 50% of these women had fewer than five mammograms during this period.

Many Tumors Were Found as Palpable Masses in Women with No Record of an Earlier Mammogram

Approximately 25% of the invasive breast tumors in the MGH data set (204 never-screened tumors in a total of 810 tumors; see Table 1) were identified on clinical grounds in women for whom there was no record of mammography prior to the appearance of the clinical sign.[8] These never-screened tumors were larger, with a median size of 15 mm and, thus, were more likely to be lethal than the screen-detected tumors (first screen-detected tumors and subsequent screen-detected tumors), with a median size of 10 mm (Table 1).[8]

Failure to Achieve Prompt Compliance with the Annual Screening Recommendation Resulted in the Appearance of Many Tumors Long after the Previous Negative Screening Mammogram

One hundred twenty-five of 312 (40%) mammographically detected invasive tumors that were found in women with a previous negative mammogram (subsequent screen-detected tumors; see Table 1) were found more than 1.5 years after the previous negative mammogram, and 86 of 312 (≈33%) were identified more than 2 years after (Figs. 4, 5). Eighteen of 132

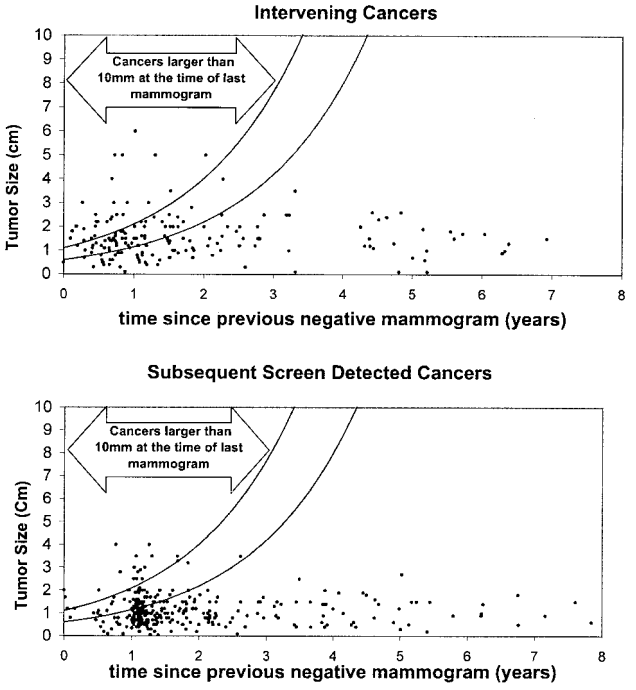

FIGURE 4. Scatter plots showing the sizes of tumors found after a previous negative mammogram compared with the time since the previous negative mammogram. Also shown are the theoretical growth curves (see Eq. 1, Materials and Methods) for tumors measuring 5 mm and 10 mm growing with a doubling time of 130 days.[11–16] Thus, most of the tumors located below the bottom line were likely to have been 5 mm or smaller at the time of the previous negative mammogram, whereas tumors below the top line were likely to have been 10 mm or smaller at the time of the previous negative mammogram. (Top) Tumors found by nonmammographic detection in women with a previous negative mammogram (intervening tumors; the results from two women who had tumors with time $>$ 8 years since the previous negative mammograms were omitted). (Bottom) Tumors found by mammographic detection in women with a previous negative mammogram (subsequent screen-detected tumors; results from two women who had tumors with time $>$ 8 years since the previous negative mammograms were omitted).

(6%) mammographically detected invasive tumors were found more than 5 years after the last previous negative mammogram, and the longest period for the subsequent screen-detected tumors in the MGH data set was 10.42 years.

Seventy-eight of 179 (44%) nonmammographically detected invasive tumors that were found in women with a previous negative mammogram (intervening tumors; see Table 1) were found more than 1.5 years after the previous negative mammogram, and 56 of 179 tumors (≈33%) were identified more than 2 years after (Figs. 4, 5). Twenty-six of 179 (15%) nonmammographically detected invasive tumors were found more than 5 years after the last previous negative mammogram, and the longest period for intervening tumors in the MGH data set was 13.8 years (Figs. 4, 5).

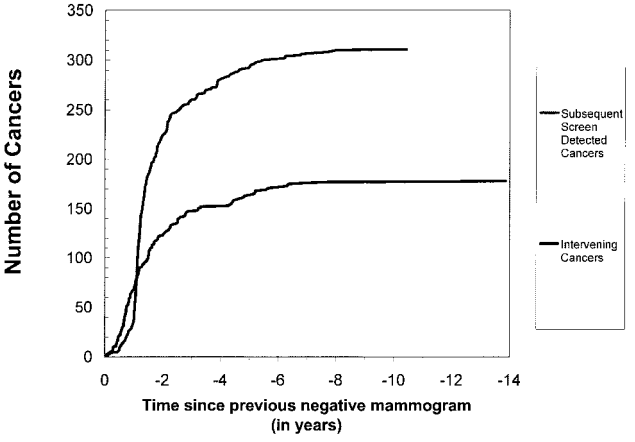

FIGURE 5. Time since previous negative mammogram, in years, for patients with subsequent screen-detected and intervening tumors.

Most Nonmammographically Detected Tumors in the Screening Population (Intervening Tumors) Probably Would Have Been Found at a Smaller Size If Screening Had Been Carried Out More Frequently

The impact of the 179 nonmammographically detected invasive tumors that were found in women with a previous negative mammogram (intervening tumors) is demonstrated by the fact that they constituted approximately 30% of the 604 invasive breast tumors in the screening population (intervening, subsequent screen-detected, and first screen-detected tumors) (Fig. 6). These intervening tumors tended to be larger (median, 15 mm) than the screen-detected tumors (median, 10 mm; see Table 1 and Michaelson et al.[8]). However, although the 179 intervening tumors made up approximately 30% of the invasive tumors in the screening population, only 21 tumors (3%) were found within 6 months of the previous negative examination, and only 46 tumors (9%) were found in the period from 6 months to 12 months (Fig. 6). Furthermore, the few intervening tumors that were found within 1 year of the previous mammogram tended to be slightly smaller (median, 14 mm; mean, 15.5 mm) than the intervening tumors that were found after that time (median, 15 mm; mean, 17.6 mm) (Table 1). Note that the 2-mm difference in greatest dimension corresponds to a 33% reduction in volume and cell number, assuming equivalent spherical geometry and cellular density.

Two findings suggest that most of the 179 intervening tumors probably would have been found at smaller sizes at screening if the women with these

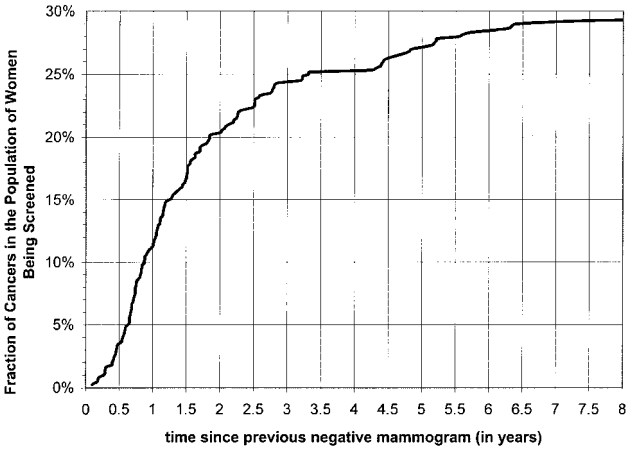

FIGURE 6. The appearance over time of the nonmammographically detected tumors found in women with a previous negative mammogram (intervening tumors) as a fraction of the tumors in the screening population (intervening tumors, subsequent screen-detected tumors, and first screen-detected tumors).

tumors had returned promptly for their mammographic examinations. First, in almost all patients who had diagnostic mammography at the time of detection of these palpable tumors, signs of breast carcinoma were found on the mammogram. This was the case for all of the intervening tumors that were found within 6 months of the previous negative mammogram, for 96% of the intervening tumors that were found from 6 months to 1 year after the previous negative mammogram, and for 82% of the intervening tumors that were found between 2 year and 3 years after the previous negative examination. Second, by using Equation 3 to estimate the sizes of intervening tumors at the time of the previous mammogram (assuming an average doubling time of 130 days based on estimates from this laboratory; our unpublished results and other reports[11–16]), it appears that most of these tumors probably were too small at the time of the negative mammogram to have been candidates for detection (Fig. 4, top). Indeed, 75 of 179 intervening tumors (42%) were likely to have been 5 mm or smaller at the time of the previous negative mammogram, whereas 150 of 179 intervening tumors (84%) were likely to have been 10 mm or smaller at that time (Fig. 4 top). Thus, the reason why most of these intervening tumors emerged as larger palpable masses was not that they were *missed* at the previous negative mammogram (because most were too small at that time to have been detected) but because too much time had been allowed to pass since the previous negative mammogram.

DISCUSSION

The current findings describe the pattern of screening utilization and its consequences, in terms of invasive breast tumor size and time of tumor appearance, among women who were examined at the MGH Breast Imaging Center over the last decade. These findings reveal that utilization of breast cancer screening is far from optimal despite the fact that, for the past 2 decades, the MGH Breast Imaging Division has vigorously recommended prompt compliance with annual screening from age 40 years onward. About 1 in 4 of the 810 invasive breast tumors in the MGH data set were found in women for whom there was no record of a previous screening mammogram, and these tumors were larger (median size, 15 mm) and, thus, more likely to be lethal than the screen-detected tumors (median size, 10 mm). About 50% of the women who used screening did not begin until age 50 years, although approximately 25% of the invasive breast tumors in the data set were found in women younger than age 50 years.[8] Few of the women who used screening returned promptly for their annual examinations, a finding in general agreement with other studies of this type.[17–22] Only approximately 50% of the women who underwent screening at MGH had returned by 1.5 years, and only approximately 60% had returned by 2 years. Because of this incomplete utilization, many tumors appeared at larger and thus, presumably, more lethal sizes than would have been the case if there had been more widespread adherence to the ACS recommendation of prompt annual screening from age 40 years.

It is striking that 179 of 604 (≈30%) invasive breast tumors in the screening population emerged at larger sizes as nonmammographically detected intervening tumors, mostly as palpable masses. However, only 3% of the 604 tumors in the screening population were found as intervening tumors within 6 months of the previous negative examination, whereas only 9% were found in the period from 6 months to 12 months. These values are remarkably similar to those reported by Mandelson et al.,[23] who found that, although 28% of the tumors in a health maintenance organization screening population were seen on nonmammographic grounds within 24 months of the previous negative examination, only 11% were found within 12 months, and Kelikowski et al.,[24] who found that 12% of the invasive tumors in a mobile mammography screening population were seen on nonmammographic grounds within 13 months of the previous negative examination, whereas only 3% were found within 7 months. Almost all of the intervening tumors in our data set were demonstrable by mammography

at the time they were discovered. Furthermore, by back-calculating the likely sizes of these tumors at the time of the previous negative mammogram (using the median tumor doubling-time of 130 days based on a variety of studies[11–16]), it could be seen that most of these tumors probably were too small at that time to have been candidates for detection. (It has been suggested that intervening tumors may have growth rates faster than the median value;[23] if this is true, then even fewer of these tumors should have been large enough at the time of screening to have been in the range of mammographic detectability.) Apparently, the reason why most of the intervening tumors in the MGH data set emerged after the negative mammogram was not the failure to detect them mammographically but because too much time had been allowed to elapse. Thus, the 30% of tumors that emerged as palpable masses in women with a previous negative mammogram may have been reduced to as low as 12% if screening had been carried out at prompt yearly intervals or reduced to as low as 3% if the screening occurred every 6 months.[25]

Taken together, the current findings suggest that far too many women in the MGH data set did not comply with the ACS recommendation of prompt annual screening and that, as a result, almost 50% of the invasive tumors emerged as larger, potentially more lethal, palpable masses rather tumors of smaller size that may have been found at screening. Furthermore, these disappointing findings probably underestimate the national failure to utilize breast cancer screening to its fullest benefit, because Massachusetts has among the highest self-reported rates of utilization in the nation.[26] Thus, the data presented here suggest that prompt annual screening would have provided a substantial reduction in the sizes of the many of the tumors found among the patients in the data set. Understanding why women fail to utilize breast cancer screening as recommended and finding ways to encourage prompt annual screening from the age of 40 years may lead to considerable reductions in death from breast carcinoma, and such efforts should have a high priority.

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