

A Comparison of Ink-Directed and Traditional Whole-Cavity Re-Excision for Breast Lumpectomy Specimens With Positive Margins

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Background: Excising a breast tumor with negative margins minimizes local recurrence. With a positive margin, the standard re-excision consists of excising the whole cavity and all surrounding breast tissue. By marking the sides of the lumpectomy specimen with six different colored inks, the surgeon can limit the re-excision to the involved margin. We compared the local recurrence rate after these two re-excision methods.

Methods: Records were reviewed of 527 women (546 breasts) treated with lumpectomy at two institutions. The log-rank test was used to compare the local recurrence-free survival.

Results: Of 546 tumors, 245 (45%) had negative margins on the initial lumpectomy and were not re-excised. Fifty-five percent had a positive or close margin; 181 underwent whole-cavity re-excision, and 120 had ink-directed re-excision. The mean follow-up time was 3.4 years. There was no significant difference in local recurrence for the patients whose initial margin was negative (3.7%) compared with the 243 patients with initially positive margins who underwent a re-excision (3.3%). Eleven of 181 (6%) patients undergoing a whole-cavity re-excision developed a local recurrence, compared with none of 120 (0%) patients with an ink-directed re-excision ($P =$ not significant). Tissue mass excised was significantly smaller in the ink-directed group (23 vs. 83 g, $P < .05$).

Conclusions: Ink-directed re-excision of lumpectomy specimens with positive margins minimizes the amount of breast tissue removed without increasing the incidence of local recurrence and is therefore preferable to the standard whole-cavity method.

Key Words: Breast cancer—Ductal carcinoma in situ—Surgery—Margins.

The goal of breast-conserving treatment of invasive breast cancer and ductal carcinoma in situ (DCIS) is to minimize the chance that the tumor will locally recur in the breast while maximizing cosmetic outcome. The most important determinant of local tumor recurrence in patients treated with lumpectomy and radiotherapy is the presence or absence of tumor at the surgical margin of resection: patients with invasive carcinoma or DCIS at the margin are at least 2- to 3-fold more likely to develop

a local recurrence than patients with negative margins.^{1–3} Therefore, when tumor is found to be present at the margin of a lumpectomy specimen, re-excision to obtain a negative margin is indicated. Recent studies with long follow-up provide evidence that the margin width is also an important determinant of local tumor recurrence in patients with DCIS⁴ and invasive cancer,^{1,5,6} leading some to recommend re-excision when the initial lumpectomy margin is close.

Because many patients will require re-excision, we have evaluated an ink-directed method of re-excision that allows one to obtain negative margins and at the same time minimize the amount of breast tissue removed. Often a breast cancer lumpectomy specimen is sent to pathology, where the pathologist marks it with a single color of ink. This single-color ink technique allows assessment of tumor proximity to the margin but

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does not indicate the spatial orientation of a close or focally positive margin. In this scenario, the surgeon must then re-excise tissue around the entire cavity left by the lumpectomy to ensure that the residual tumor focus is removed. This whole-cavity re-excision has been the traditional method of dealing with a positive margin. An alternative approach, described by Cady,⁷ uses a system of six multicolored inks. In the operating room, the surgeon uses a different color to mark each of six surfaces (superficial, deep, cranial, caudal, medial, and lateral) of the excised lumpectomy specimen (Fig. 1). These colored inks persist on the final pathology slides. When faced with a positive margin, the surgeon then knows the specific location in the original biopsy cavity that requires re-excision. This ink-directed re-excision enables the surgeon to re-excise only the involved margin, therefore minimizing the amount of breast tissue removed. Because it has been well established that cosmetic outcome is directly related to the volume of tissue removed during breast conserving surgery,⁸⁻¹² it is likely that ink-directed re-excisions would yield better cosmetic results than traditional whole-cavity re-excisions.

To our knowledge there has been no reported comparison between this ink-directed method and the traditional whole-cavity technique for re-excising lesions with pos-

itive margins. We therefore initiated this study to compare the local recurrence rates of breast cancer patients treated with these two different re-excision techniques.

METHODS AND MATERIALS

After obtaining institutional review board approval, we retrospectively reviewed the medical records of (1) all breast cancer patients who had breast-conserving therapy at Dartmouth-Hitchcock Medical Center from February 1990 to June 1999 and (2) all breast cancer patients identified by a tumor registry database to have been treated with breast-conserving surgery by three surgeons at the Beth Israel Deaconess Medical Center from 1982 to 1999. Clinical data collected included patient age, tumor size, tumor type, mammographic detectability, margin status of the initial excision and re-excisions, type of re-excision performed, number of re-excisions, weight of the re-excision specimens, adjuvant therapy received, and patient outcome with respect to local and in-breast recurrence and survival. Margins were considered negative if there were no cancer cells seen at the edge of the resection. Patients were examined for recurrence at least semiannually. Mammograms were generally obtained every 6 months for the first 2 years

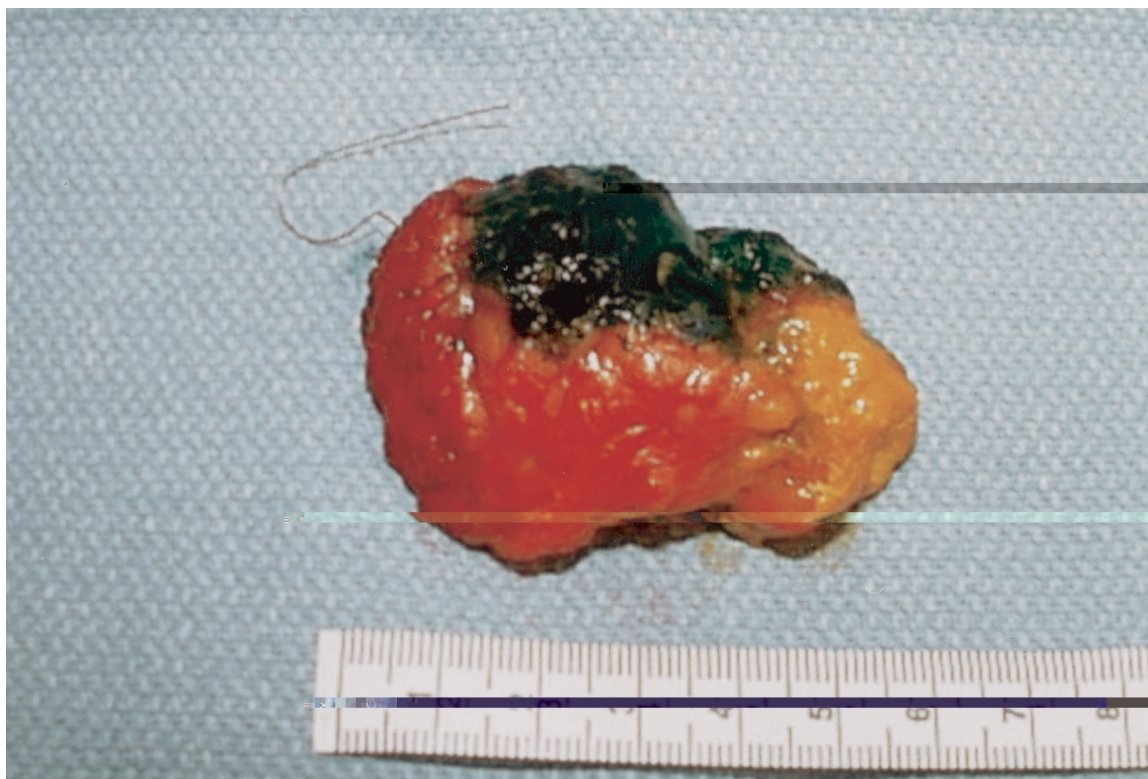


FIG. 1. Lumpectomy specimen marked with six different colored inks for spatial orientation.

and annually thereafter. Local failure was defined as a recurrence adjacent to the initial lumpectomy site or in the same quadrant as the initial lumpectomy. In-breast recurrence was defined as any subsequent tumor arising in the breast at a site distant from the initial lumpectomy.

The whole-cavity re-excision technique consisted of an excision of a few millimeters of skin around the initial lumpectomy site incision, followed by excision of at least 1 cm of tissue around the entire cavity left by the lumpectomy. The initial lumpectomy specimens from patients who were treated with ink-directed re-excisions were marked with six different colored inks (Davidson Marking System™, Bradley Products, Inc., Bloomington, MN). Ink-directed re-excisions were performed by opening the previous lumpectomy incision (not excising the skin) and excising at least 1 cm of tissue from the sides of the cavity that corresponded to the positive lumpectomy margins.

Survival curves for each clinical end point were estimated with the Kaplan-Meier method, by using the log-rank test to compare patient groups. Relative risks (RR) and 95% confidence intervals (CI) were computed on the basis of proportional hazard regression analysis.

RESULTS

The study population consisted of 527 women who underwent 546 lumpectomies for breast malignancies; invasive tumors were found in 453 (83%) of the speci-

mens, and only DCIS was found in the remaining 93 specimens. Two hundred forty-five lumpectomies had negative initial margins and no re-excision; the remaining 301 lumpectomies (55%) underwent re-excision. As shown in Fig. 2, the percentage of patients who have undergone a re-excision has remained fairly constant (roughly 50%) over the time period of the study. The great majority (243 of 301 [81%]) of the patients who underwent re-excision did so because of a positive margin on the initial lumpectomy. As shown in Fig. 2, the percentage of patients with positive margins after the initial lumpectomy has also stayed relatively constant over the time course of the study.

One hundred twenty (40%) of the 301 patients who underwent re-excision had an ink-directed re-excision, and 181 had the standard whole-cavity re-excision. Figure 3 illustrates that the proportion of patients undergoing ink-directed re-excisions has been increasing over time. Ink-directed re-excisions began to be performed at the Deaconess Hospital in the early 1990s and were adopted as the standard procedure at Dartmouth-Hitchcock in late 1996. By 1999, >80% of the re-excisions performed at both institutions were ink directed. Because both institutions are referral hospitals, a sizable number of patients are referred for definitive therapy after having an initial lumpectomy with a positive margin at an outside institution where the edges were not marked with different colors of ink. Of necessity, because the partic-

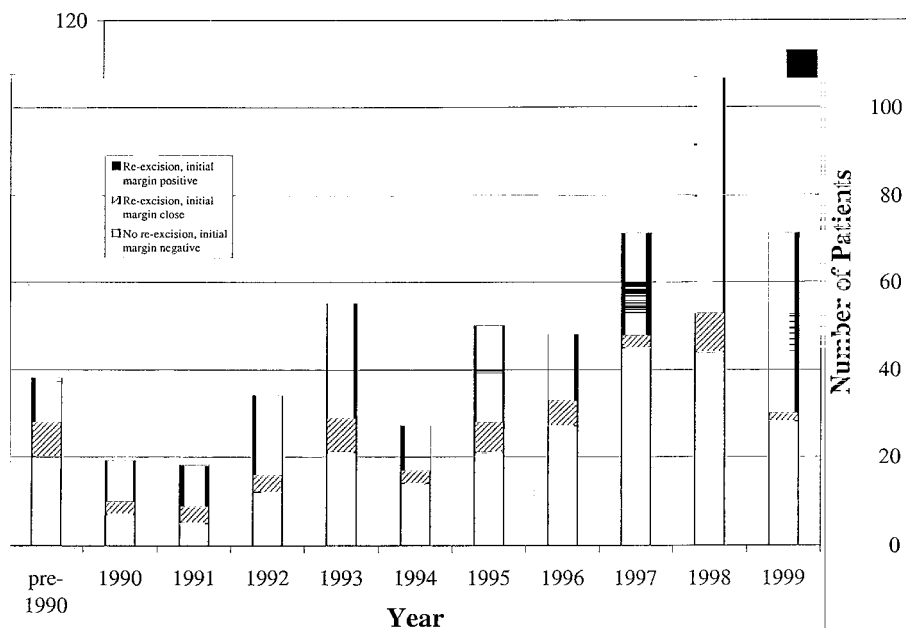


FIG. 2. Composition of the study groups based on re-excision status.

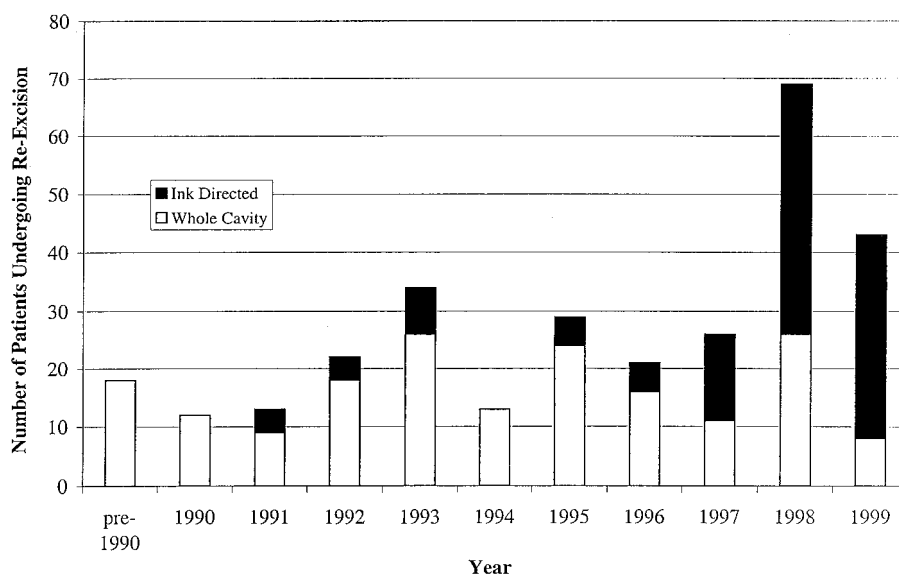


FIG. 3. Number of patients per year who underwent ink-directed or whole-cavity re-excision.

ular positive margin is not known, these patients continue to be treated with whole-cavity re-excisions.

Characteristics of the patients who had initially negative margins and had no re-excision or underwent ink-directed or whole-cavity re-excision are listed in Table 1. There were no statistically significant differences among the three groups regarding the size of the primary tumor, number of re-excisions required to achieve a negative margin, and type of adjuvant therapy administered. Patients in the ink-directed group were more likely to have had a positive margin on the initial lumpectomy when compared with patients in the whole-cavity re-excision group (104 of 120 [87%] vs. 139 of 181 [77%]; $P = .03$). There were also significant differences between the

groups in mean patient age (with the ink-directed group slightly younger than the initial-margin-negative group) and type of tumor (a significantly higher percentage of DCIS in the ink-directed group). In univariate analysis, none of these variables (percentage of patients with positive margins on the initial lumpectomy, patient age, or tumor type) had a significant effect on the proportion of patients who developed a local or in-breast recurrence over time.

Because the mean follow-up time for the ink-directed re-excision group is shorter than for the other groups, we controlled our analysis for this by using the log-rank test to assess for differences between the groups in the proportion of patients who developed a local recurrence

TABLE 1. Characteristics of the study group based on re-excision status

Variable	Initial margin negative, no re-excision	Ink-directed re-excision	Whole-cavity re-excision
Total number of patients	245	120	181
Patient age, y (SD)	60.2 (13.0)	55.1 (11.1)	56.6 (12.5)
Mean tumor size, cm (SD)	1.47 (0.98)	1.35 (0.90)	1.44 (0.82)
Tumor histology			
Invasive ductal (%)	191 (78)	78 (65)	145 (80)
Invasive lobular (%)	22 (9)	10 (8)	7 (4)
DCIS (%)	32 (13)	32 (27)	29 (16)
Patients with positive margins on initial lumpectomy (%)	—	104 (87)	139 (77)
Patients with two re-excisions (%)	—	12 (10.0)	21 (11.6)
Adjuvant therapy			
None (%)	41 (16.7)	22 (18.3)	35 (19.3)
XRT ± systemic therapy (%)	194 (79.2)	97 (80.8)	141 (77.9)
Systemic therapy only (%)	10 (4.1)	1 (0.8)	5 (2.8)
Mean follow-up time, y (SD)	3.3 (2.5)	2.0 (1.2)	4.5 (2.7)

DCIS, ductal carcinoma in situ; XRT, radiotherapy.

over time. Figure 4 shows the proportion of patients in each of the three groups who experienced a local recurrence. At 4 years, the percentages of patients who developed a local recurrence in the negative-margin no-re-excision group and in the whole-cavity and ink-directed re-excision groups were 2.8%, 5.8%, and 0%, respectively. There was no statistically significant difference in the proportion of patients who developed a local recurrence when the patients with initially negative margins and no re-excision and the patients who underwent whole-cavity re-excision or ink-directed re-excision were compared.

Over the entire period of the study, 9 of 245 (3.7%) patients with initially negative margins and no re-excision had a local recurrence, compared with 11 of 181 (6.1%) patients who underwent a whole-cavity re-excision and none of 120 patients undergoing an ink-directed re-excision (Table 2). A small number of patients developed a second tumor in a quadrant distant from the site of the first tumor. These patients were added to the patients who experienced local recurrences to determine the total number of patients with an in-breast recurrence, as shown in Table 2. There was no difference in the proportion of patients who developed an in-breast recurrence over time when patients with initially negative lumpectomy margins and no re-excision, patients who underwent ink-directed re-excisions, and those who had whole-cavity re-excision were compared. When compared with the whole-cavity re-excision group, the RR of

recurrence of the ink-directed re-excision group was .51 (95% CI, .11–2.31).

A total of 24 of the patients treated at Dartmouth-Hitchcock Medical Center had their re-excision specimens weighed by the pathologist. Fourteen of the patients had whole-cavity re-excisions, and 10 had ink-directed re-excisions. The mean weight of the whole-cavity re-excision specimens was 83 g, almost 4-fold larger than the mean weight of the ink-directed re-excision specimens (23 g; $P = .01$; Fig. 5).

In addition, we noted that there was no significant difference in the RR of local recurrence when the 243 patients with an initially positive margin that was re-excised to achieve a negative margin (by either method) were compared with the 245 patients with an initially negative margin who had no re-excision (RR = 1.02; 95% CI, .41–2.52). Nine of 245 (3.7%) patients with initially negative margins had recurring tumors, compared with 10 of 243 (3.3%) patients with initially positive margins who underwent re-excision. This relationship held for the subgroup of patients with invasive cancer and for the subgroup of patients with DCIS.

Patients With Invasive Cancer

We separately analyzed the 453 patients with invasive breast cancers, and the descriptive characteristics of these patients are listed in Table 3. There were no significant differences between the groups with regard to the size of the primary tumor, histological type of tumor

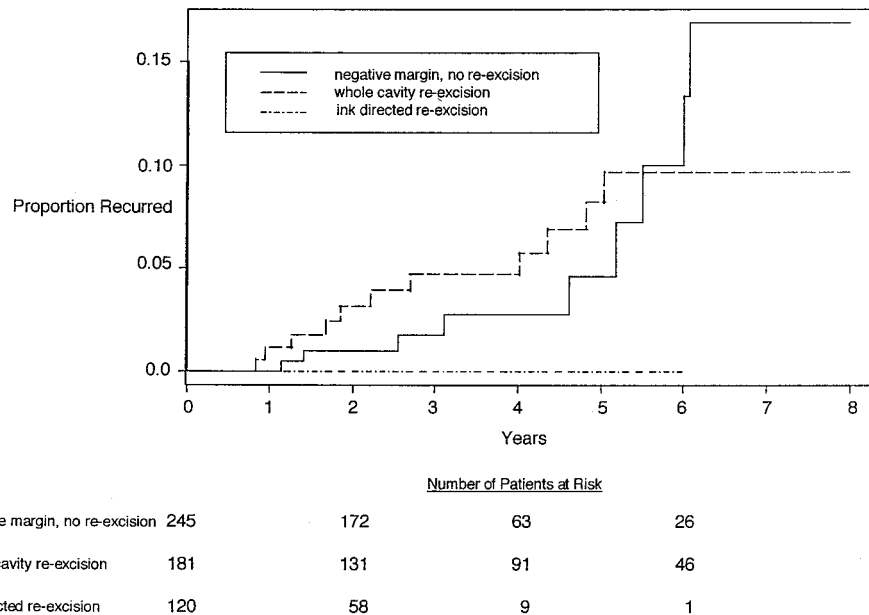


FIG. 4. Proportion of patients in the study who developed a local recurrence.

TABLE 2. Incidence and relative risk of recurrence for all patients in the study

Variable	Initial margin negative, no re-excision	Whole-cavity re-excision	Ink-directed re-excision
No. patients	245	181	120
Local recurrence (%)	9 (3.7)	11 (6.1)	0
In-breast recurrence (%)	11 (4.5)	15 (8.3)	2 (1.7)
Relative risk of in-breast recurrence (95% CI)	—	—	.51 (.11–2.31)

The relative risk of in-breast recurrence in the ink-directed re-excision group was compared with the whole cavity re-excision group. CI, confidence interval.

(lobular vs. ductal), number of re-excisions required to achieve a negative margin, and type of adjuvant therapy administered. Patients in the ink-directed re-excision group were more likely to have had a positive margin on the initial lumpectomy when compared with the patients in the whole-cavity re-excision group (78 of 88 [89%] vs. 118 of 152 [78%], $P = .03$). There was also a significant difference between the groups in mean patient age (with the ink-directed re-excision group slightly younger than the initial-margin-negative, no-re-excision group). In univariate analysis, neither patient age nor the presence of positive margins on the initial lumpectomy specimen affected the proportion of patients developing a local or in-breast recurrence over time.

To determine whether the ink-directed re-excision technique accurately identified and led to the removal of residual tumor, we compared the proportion of patients with a positive invasive cancer margin on the initial lumpectomy who were found to have residual cancer in the ink-directed and whole-cavity re-excision specimens. There was no significant difference in the percentage of patients found to have cancer in an ink-directed re-excision (41%) when compared with a whole-cavity re-excision (49%), thereby indicating that we are reliably identifying the site of residual cancer with this technique (Fig. 6).

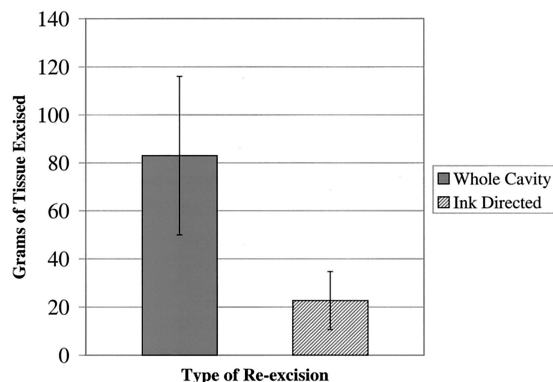
**FIG. 5.** Mean mass of the specimens re-excised with each technique.

Figure 7 shows the proportion of patients with invasive cancer who developed a local recurrence. At 4 years, the percentages of patients developing a local recurrence for the negative-margin, no-re-excision group and the whole-cavity or ink-directed re-excision groups were 1.4%, 4.7%, and 0%, respectively. There was no difference in the proportion of patients developing a local recurrence when the patients with initially negative margins and no re-excision, the patients undergoing whole-cavity re-excision, and the patients undergoing ink-directed re-excision were compared. The absolute number of patients over the entire time of the study who developed a local or in-breast recurrence in each of these groups is shown in Table 4. There was no statistically significant difference in the RR of in-breast recurrence in these three groups of patients. When compared with the whole-cavity re-excision group, the RR of in-breast recurrence for the ink directed group was .54 (95% CI, .07–4.47).

There was no difference in mortality among the three groups. Compared with the group of patients with negative initial margins and no re-excision, the RR of death for the ink-directed group was .36 (95% CI, .05–2.82); for the whole-cavity group, the RR was .79 (95% CI, .37–1.67).

Of the patients with invasive cancer, 386 (85.2%) received radiation alone or in conjunction with chemotherapy (Table 3). Figure 8 shows the proportion of patients with invasive cancer who received adjuvant radiotherapy and developed a local recurrence. Over the entire duration of the study, the local and in-breast recurrence rates for the patients who had an initial negative margin and no re-excision and who then received radiation were both 2.3%. The corresponding local and in-breast recurrence rates for patients who had an ink-directed re-excision and radiation were 0% and 1.3%, and for those who had a whole-cavity re-excision and radiation they were both 2.3%. Analysis of the proportion of patients with invasive cancer who received adjuvant radiotherapy and developed local or in-breast recur-

TABLE 3. Characteristics of the patients with invasive cancer, based on re-excision status

Variable	Initial margin negative, no re-excision	Ink-directed re-excision	Whole-cavity re-excision
Total number of patients	213	88	152
Patient age, y (SD)	60.0 (13.0)	55.2 (11.0)	56.4 (12.5)
Mean tumor size, cm (SD)	1.53 (0.99)	1.45 (0.84)	1.47 (0.83)
Tumor histology			
Invasive ductal (%)	192 (90)	78 (89)	144 (95)
Invasive lobular (%)	21 (10)	10 (11)	7 (5)
Patients with positive margins on initial lumpectomy (%)	–	78 (89)	118 (78)
Patients with two re-excisions (%)	–	7 (8.0)	16 (10.5)
Patients with tumor in re-excision specimen (%)	–	36 (40.9)	75 (49.3)
Adjuvant therapy			
None (%)	28 (13.1)	9 (10.2)	18 (11.8)
XRT ± systemic therapy (%)	176 (82.6)	78 (88.7)	132 (86.9)
Systemic therapy only (%)	9 (4.2)	1 (1.1)	2 (1.6)
Mean follow-up time, y (SD)	3.4 (2.5)	2.1 (1.3)	4.5 (2.7)

XRT, radiotherapy.

rence did not demonstrate any significant differences among the three treatment groups.

A total of 10 patients with invasive breast cancer underwent an ink-directed re-excision (without skin re-excision) and did not receive adjuvant radiotherapy. We observed no skin or local recurrences in these patients.

Patients With DCIS

We separately analyzed the 93 patients who were found to have solely DCIS in their initial lumpectomy specimen, and the descriptive characteristics of these patients are listed in Table 5. There were no significant differences between the groups with regard to patient age, pathologic size of the primary tumor, number of re-excisions required to achieve a negative margin, and type of adjuvant therapy. There was no significant difference between the ink-directed and whole-cavity re-excision groups with regard to the percentage of patients who had a positive margin on the initial lumpectomy (ink

directed, 26 of 32 [81%] vs. whole cavity, 21 of 29 [72%]).

The proportions of the patients with DCIS who had an initial negative margin and no re-excision, or who underwent ink-directed or whole-cavity re-excision and developed a local recurrence, are shown in Fig. 9. There was no difference among the local recurrence rates of these three groups of patients. The absolute numbers of patients who developed a local or in-breast recurrence in each of the groups are listed in Table 6. There were no local recurrences in the ink-directed re-excision group. When compared with the whole-cavity re-excision group, the RR of in-breast recurrence for the ink-directed group was .42 (95% CI, .05–3.79).

Of the patients with DCIS, 46 (49.5%) received radiotherapy, with or without tamoxifen. The local and in-breast recurrence rates for the patients with an initial negative margin (and hence no re-excision) and radiation were both 5.6%. The local and in-breast recurrence rates for the group that had an ink-directed re-excision plus radiation were both 0%. The rates of local and in-breast recurrence for patients who had a whole-cavity re-excision plus radiation were both 0%. For the patients with DCIS who were treated with radiotherapy, there was no difference in the proportion of patients developing a local or in-breast recurrence when patients with initially negative margins and no re-excision and patients undergoing ink-directed or whole-cavity re-excision were compared.

DISCUSSION

In this multi-institutional study involving multiple different surgeons, we have shown that an ink-directed

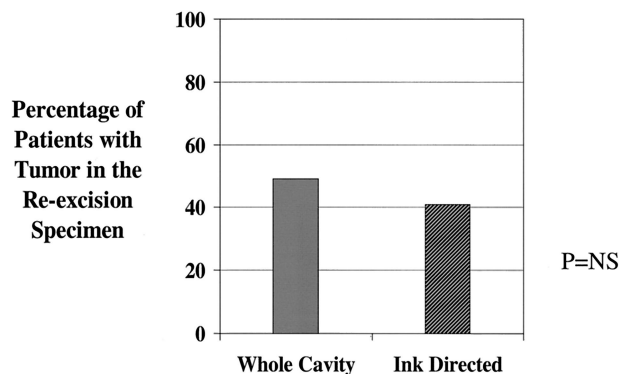
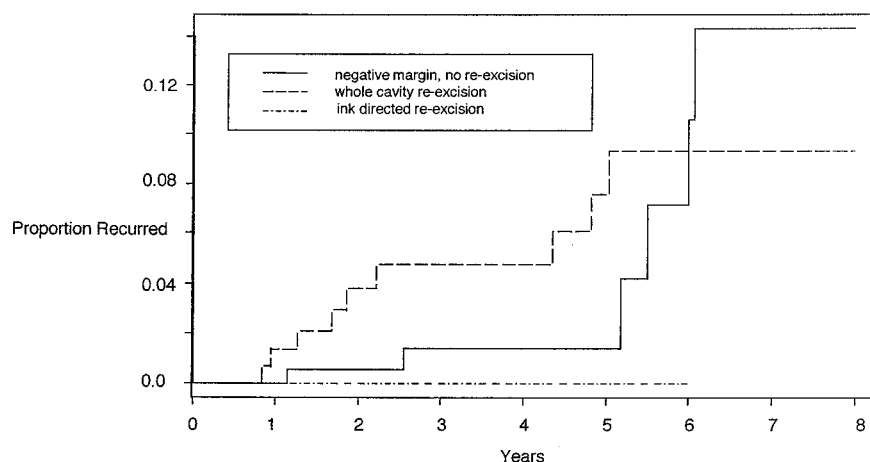


FIG. 6. The ink-directed technique accurately identifies residual tumor.



	Number of Patients at Risk			
Negative margin, no re-excision	213	156	58	26
Whole cavity re-excision	152	109	76	41
Ink directed re-excision	88	45	8	1

FIG. 7. Proportion of patients with invasive cancer who developed a local recurrence.

lumpectomy re-excision method that removes approximately one fourth of the tissue of the traditional re-excision technique results in an incidence of local tumor recurrence that is at least as good as the traditional whole-cavity re-excision method. Our findings apply both to patients with invasive cancer and to those with DCIS.

Although this was not a randomized prospective study, the ink-directed and the whole-cavity re-excision groups were fairly well matched with regard to variables that might influence the local recurrence rate. The ink-directed group did have a higher proportion of patients with positive margins on the initial lumpectomy and had a higher percentage of patients with DCIS, and this might lead one to expect a higher risk of local recurrence in this group. However, in our study population, by univariate analysis, neither of these two variables had a significant affect on the proportion of patients who developed a local or in-breast recurrence. Although the mean fol-

low-up time for the ink-directed excision group is relatively short (2.0 years), the absence, to date, of any local recurrences in 120 patients treated with a re-excision by using this technique strongly suggests that the long-term incidence of local recurrence in these patients will continue to be at least as low as patients treated with a whole-cavity re-excision.

Our finding of tumor in the re-excision specimens of 46% of the patients with positive margins on their initial lumpectomy agrees with the findings of others.^{13,14} There was no significant difference in the percentage of patients with invasive cancer and a positive margin found to have cancer in an ink-directed re-excision (41%) when compared with a whole-cavity re-excision (49%), thereby indicating that we are reliably identifying the site of residual cancer with this technique.

The process of applying six different colors of ink to the lumpectomy specimen is a simple procedure that takes <5 minutes. We believe that this is best performed

TABLE 4. Incidence and relative risk of recurrence for patients with invasive cancer

Variable	Initial margin negative, no re-excision	Whole-cavity re-excision	Ink-directed re-excision
Number of patients	213	152	88
Local recurrence (%)	6 (2.8)	9 (5.9)	0
In-breast recurrence (%)	7 (3.3)	9 (5.9)	1 (1.1)
Relative risk of in-breast recurrence (95% CI)	—	—	.54 (.07–4.47)

CI, confidence interval.

The relative risk of in-breast recurrence in the ink-directed re-excision group was compared with the whole-cavity re-excision group.

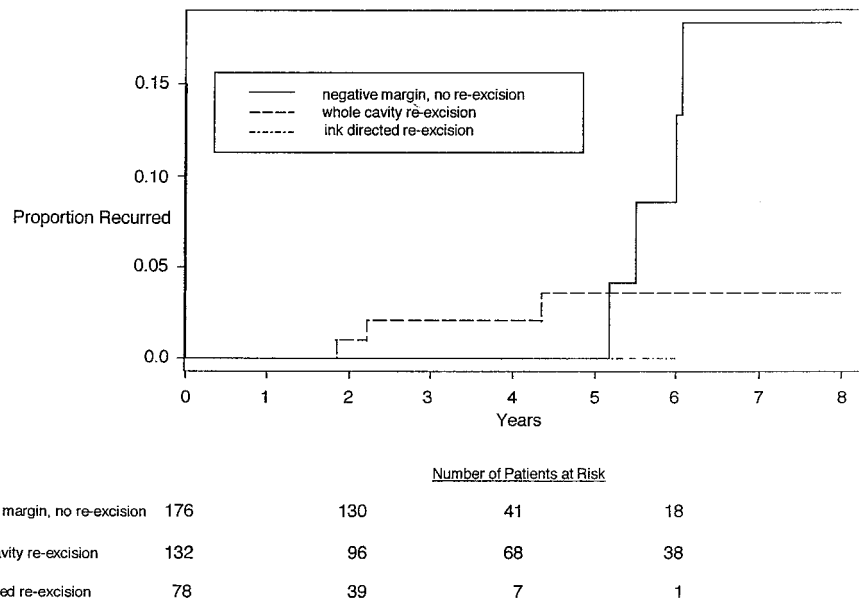


FIG. 8. Proportion of patients with invasive cancer who received adjuvant radiotherapy and who then developed a local recurrence.

by the surgeon in the operating room (rather than by a pathologist, who may receive a specimen oriented with a couple of sutures) because it minimizes chances for any error in orientation.

Excision of the skin around the scar at the time of a lumpectomy re-excision typically increases the size of the scar by at least 1 cm. It is important to note that unless the superficial margin of the original lumpectomy was positive, we did not re-excise the skin when performing re-excisions in this study. Theoretically, it did not make sense to re-excise the skin if we were not going to be re-excising other walls of the cavity that were also potentially exposed to tumor cells at the original lumpectomy. Because we did not find an increased rate of skin or local recurrence in the ink-directed re-excision pa-

tients, this practice is justified. Because 81% of our ink-directed re-excision patients were treated with adjuvant radiotherapy, it may be that radiation is capable of eradicating any micrometastases left in the skin. Is it safe to not re-excise the skin after a lumpectomy when no radiotherapy is to be administered? This is potentially relevant for patients who have had a diagnostic lumpectomy and then desire a skin-sparing mastectomy. We observed no skin or local recurrences in our small cohort of 23 patients who had an ink-directed re-excision (without skin re-excision) and did not receive adjuvant radiotherapy. This suggests that skin excision is not necessary in these patients.

In the treatment of invasive breast cancer patients with breast-conserving surgery and radiotherapy, 22 studies

TABLE 5. Characteristics of the patients with ductal carcinoma in situ, based on re-excision status

Variable	Initial margin negative, no re-excision	Ink-directed re-excision	Whole-cavity re-excision
Total number of patients	32	32	29
Patient age, y (SD)	61.0 (13.3)	54.9 (11.4)	57.5 (12.9)
Mean tumor size, cm (SD)	1.07 (.88)	1.07 (1.00)	1.17 (.71)
Patients with positive margins on initial lumpectomy (%)	—	26 (81)	21 (72)
Patients with two re-excisions (%)	—	4 (12.5)	5 (17.2)
Adjuvant therapy			
None (%)	13 (40.6)	13 (40.6)	17 (58.6)
XRT only (%)	15 (46.9)	16 (50.0)	7 (24.1)
XRT + tamoxifen (%)	3 (9.4)	3 (9.4)	2 (6.9)
Tamoxifen only (%)	1 (3.1)	0 (.0)	3 (10.3)
Mean follow-up time, y (SD)	2.8 (2.2)	1.9 (.9)	4.2 (2.2)

XRT, radiotherapy.

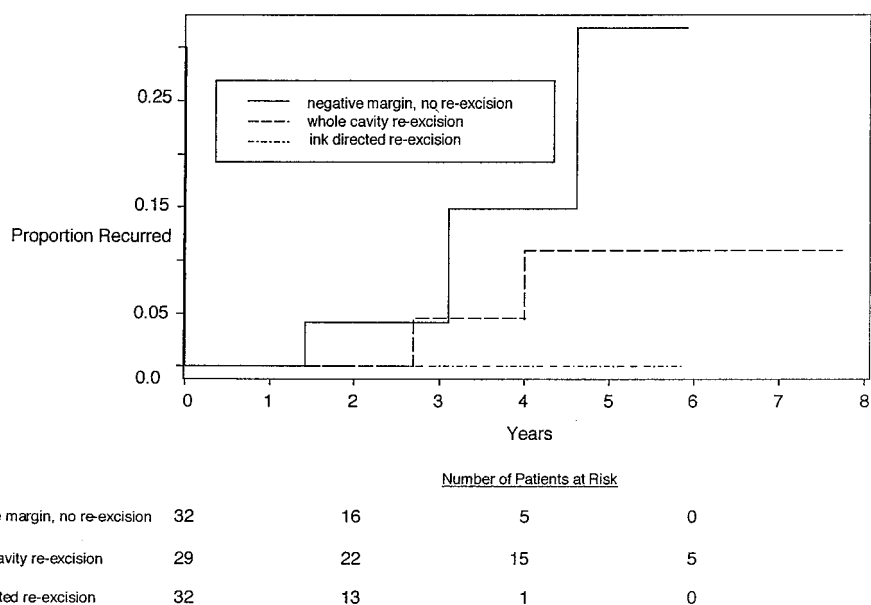


FIG. 9. Proportion of patients with ductal carcinoma in situ who developed a local recurrence.

have shown that patients with tumor at the margin are at least 2- to 3-fold more likely to develop a local recurrence than patients with negative margins (as reviewed by Freedman et al.¹ and Gage et al.²). In this study, we confirm the findings of three other studies^{1,6,15} that patients who achieve a negative margin after a re-excision have the same low risk of local recurrence as patients with an initially negative margin. These studies provide the basis for re-excising invasive breast cancer lumpectomies with positive margins.

The significance of close lumpectomy margins for patients with invasive breast cancer remains controversial. Some studies with 10-year follow-ups show that the in-breast tumor recurrence rate for patients with close (<2 mm) margins is similar to that in patients with positive margins.^{1,6,9} In contrast, Gage et al.,² with a median follow-up of 109 months, found no difference in the low local recurrence rate of patients with close (<1 mm) or negative (>1 mm) margins. If a surgeon decides to recommend a re-excision for a patient with a close

margin, an ink-directed re-excision enables the possible benefit in local control to be realized with minimal cosmetic loss.

Pathologic analysis of National Surgical Adjuvant Breast and Bowel Project-17 provides the most convincing evidence that positive lumpectomy margins are associated with an increased risk of recurrence of DCIS. In that study, the RR of recurrence for patients with uncertain or involved margins compared with that of patients with negative margins was 2.33 ($P = .004$).³ In studies by Solin et al.¹⁶ and Kestin et al.,¹⁷ the rate of in-breast recurrence in patients with a positive or close (<2 mm) margin was roughly double the rate in patients with negative margins (17% vs. 10% and 13% vs. 6%, respectively), but these differences were not statistically significant. In this study, we have now shown that there is no difference in the proportion of patients who develop a local recurrence when patients with DCIS who have an initially negative margin and no re-excision are compared with patients with an initially positive margin who

TABLE 6. Incidence and relative risk of recurrence for patients with ductal carcinoma in situ

Variable	Initial margin negative, no re-excision	Whole-cavity re-excision	Ink-directed re-excision
Number of patients	32	29	32
Local recurrence (%)	3 (9.4)	2 (6.9)	0
In-breast recurrence (%)	4 (12.5)	6 (20.7)	1 (3.1)
Relative risk of in-breast recurrence (95% CI)	—	—	.42 (.05–3.79)

The relative risk of in-breast recurrence in the ink-directed re-excision group was compared with the whole-cavity re-excision group. CI, confidence interval.

underwent re-excision to obtain a negative margin. These studies establish a rationale for re-excising patients with DCIS and positive margins.

Silverstein et al.⁴ have recently shown that the probability of local recurrence after lumpectomy for DCIS is dependent on margin width. The probability of local recurrence in 8 years for patients with DCIS treated with lumpectomy without radiotherapy whose margins were >10, 1 to 10, and <1 mm were .03, .2, and .58, respectively. Differences in the probability of local recurrence as a result of margin width were also seen in such patients treated with lumpectomy and radiotherapy (.04, .12, and .3, respectively). These data suggest that a margin width of <1 mm for DCIS may be inadequate, because even with radiotherapy, 30% of these patients have a tumor recurrence. Ink-directed re-excision is a technique that can be used to re-excise a close DCIS lumpectomy margin to optimize both the oncological and cosmetic result.

In treating a patient with breast-conserving surgery it is preferable to obtain a negative margin at the time of the initial lumpectomy. Touch prep cytology has been used to examine margins at the time of surgery by some groups.^{18,19} This allows immediate resection of more tissue if a margin is positive, but its application is limited by the need for a pathologist with considerable cytology expertise to be immediately available for all breast lumpectomies, and it will not identify patients who might be candidates for re-excision on the basis of close margins. When a woman presents with a palpable mass, performing a fine-needle aspiration or core biopsy to establish the diagnosis of cancer allows one to perform a therapeutic rather than diagnostic lumpectomy. Tartter et al.²⁰ have shown that knowing that a palpable mass was malignant before lumpectomy significantly decreased the incidence of positive margins from 90% to 58%. Others have reported that the incidence of positive margins after therapeutic lumpectomy for palpable or ultrasonographically detectable breast cancers can be as low as 5%.^{13,21} When patients present with nonpalpable, mammographically detectable lesions and undergo diagnostic needle localized lumpectomies, positive margins are found in 55% to 89% of the specimens.^{12,20,22–25} If a diagnosis of malignancy is made by core biopsy, followed by a needle localized therapeutic lumpectomy, several studies have shown that the incidence of positive margins can be decreased. For example, 0 of 7 patients,²² 2 of 19 patients (11%),²⁵ and 16 of 56 patients (29%)²³ had positive margins when a therapeutic needle localized lumpectomy was performed. In analysis of the subgroup of patients in this study with invasive cancer treated at Dartmouth, we also found that the incidence of positive

margins on the initial lumpectomy was lower if a diagnosis was known before the lumpectomy. Of 124 therapeutic lumpectomies for invasive cancer, the margin was positive in 19%, compared with positive margins in 64% of 122 diagnostic lumpectomies. Of note, however, was the high positive margin rate after both therapeutic and diagnostic lumpectomies in patients with DCIS: 9 of 22 (41%) DCIS patients had positive margins after initial therapeutic lumpectomy, whereas 7 of 17 (41%) DCIS patients also had positive margins after an initial diagnostic lumpectomy.

The reason that a lower proportion of patients has positive margins when the surgeon knows a lesion is malignant and performs a therapeutic lumpectomy, of course, is because the surgeon excises more breast tissue. This was nicely documented by Al-Sobhi et al.,²⁵ who showed that the mean volume removed after a diagnostic wire localized biopsy was 38 ml, compared with a volume of 104 ml from a therapeutic wire localized lumpectomy. Knowledge that an ink-directed re-excision can be performed with removal of only a small amount of additional tissue and that the local recurrence rate after a re-excision of a positive margin is the same as after an initial negative margin has important practical implications. It allows the surgeon to plan to resect a modest amount (approximately 1 cm) of normal tissue around the tumor at the time of the initial therapeutic lumpectomy, rather than taking significantly more breast tissue in an overly aggressive attempt to ensure negative margins.

In conclusion, we recommend that diagnostic and therapeutic lumpectomies for both DCIS and invasive breast cancer be marked with six different colors of ink by the surgeon. If a margin is positive or close, a directed re-excision can be performed. Ink directed re-excisions are superior to the standard whole-cavity excision: equivalent local tumor control is accomplished with removal of only one fourth as much breast tissue.

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