

Bilateral Breast Cancer, Clinical and Pathological Review

GEORGE G. FINNEY, JR.,* M.D., F.A.C.S., GEORGE G. FINNEY,** M.D., F.A.C.S.,
ALBERT C. W. MONTAGUE,*** M.D., F.A.C.S.,
GEARY L. STONESIFER, JR.,† M.D., F.A.C.S.,
CHARLES C. BROWN,†† M.D.

*From the Department of Surgery, Johns Hopkins University School of Medicine,
Baltimore, Maryland*

THE problem of bilateral carcinoma of the breast has been receiving increasing attention in the surgical literature,^{6, 7, 9, 11, 14} but the clinical and pathologic features which characterize patients with this disease are still being defined.

In an attempt to delineate further the characteristics of patients with bilateral breast cancer, we have collected 50 cases from our surgical group practice which have been treated and followed by us over a 35-year period. Our series is analyzed in terms of epidemiologic, pathologic, and therapeutic characteristics.

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For reprints: George G. Finney, Jr., M.D., 5820 York Road, Baltimore, Maryland 21212.

* Assistant Professor of Surgery, Johns Hopkins University School of Medicine.

** Associate Professor of Surgery Emeritus, Johns Hopkins University, School of Medicine.

*** Instructor of Surgery, Johns Hopkins University School of Medicine.

† Chief of Surgery, Greater Baltimore Medical Center; Assistant Professor of Surgery, Johns Hopkins University School of Medicine.

†† Pathologist, Greater Baltimore Medical Center.

Materials and Methods

The records of our group practice provided most of the clinical data for this review. They were supplemented by hospital records, histological slides, personal follow-up, and death records.

The clinical review includes 50 patients. The pathological review of 60 breast specimens has been limited to 30 cases in which adequate histologic materials have been available for thorough analysis of both breasts.

Epidemiological Characteristics

Family History

It has been reported by D. E. Anderson,¹ Hubbard,⁶ Kilgore,⁷ Leis *et al.*,⁸ and Robbins and Berg,¹² that the family history is more frequently positive for breast cancer in patients who have bilateral breast cancer. Twenty-four per cent of the patients in this series had positive family histories for cancer of the breast. Cancer of other sites occurring in a close relative was recorded in 22% of the patients in this series (Table 1).

Age Distribution

The age for the 50 cases of bilateral breast cancer is presented in Figure 1. The average age of these patients at the time of first

TABLE 1. *Miscellaneous Information*

A-Family history		
Breast Carcinoma		24%
Other Carcinoma		22%
B-Menopausal status		
Premenopausal		13%
Menopausal		30%
Post-Menopausal		57%

Table I (A) shows the percentage of patients in whom positive family history of cancer could be elicited.

Table I (B) shows the distribution of patients according to menopausal status among bilateral breast carcinomas.

diagnosis was 53.9 years. It is interesting to note that this average age was 7 years younger than the average for the unilateral breast cancer cases reported by Finney and Finney⁴ before this society in 1969. The younger average age coincides with the finding that more patients in the bilateral series were premenopausal or menopausal at the time of onset of their disease.

Thirteen per cent of the patients in this series were menstruating regularly. Thirty per cent were menopausal. We consider all

patients menstruating irregularly, or who have had one menstrual period within the past 12 months as menopausal. The remaining 57% were postmenopausal.

Fertility

Table 2 shows that a large percentage of the patients in this series were relatively infertile. We use this classification to include those who have had one child or were childless. Fifty-seven per cent of the bilateral carcinoma patients were relatively infertile compared with 24% which would be anticipated for women of similar ages in the United States population.¹⁰

A, B, O Blood Groups

The frequency of A, B, O blood groups for the 50 patients studied does not differ significantly from the expected ratios for the United States population.

Synchronous Tumors

Thirteen of the 50 patients had synchronous bilateral breast carcinomas. We have arbitrarily defined breast carcinomas as synchronous when the second tumor occurred within 12 months of diagnosis of the first.

Long-Term Survivorship

Ten patients with bilateral breast cancer, who survived longer than 15 years after their first mastectomy, were analyzed for unusual characteristics. Possibly an important finding was the long interval between the first mastectomy and the appearance of a contralateral breast carcinoma. The shortest interval between first and second tumors was 3.5 years, and the median interval was 12 years. There were no synchronous tumors in this group.

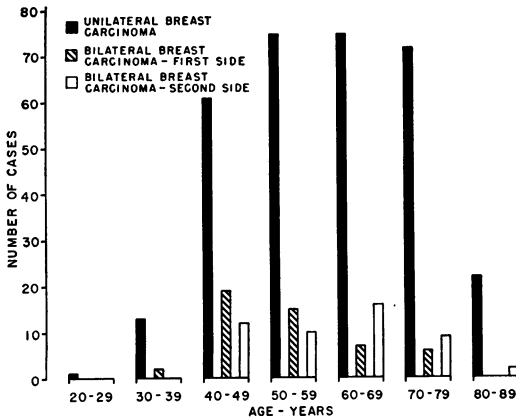


FIG. 1. Age distribution is shown comparing our series of unilateral breast carcinoma versus bilateral breast carcinoma first side and bilateral breast carcinoma second side. The average age of bilateral breast carcinoma at the time of first diagnosis was 7 years younger than for the unilateral cases.

Pathological Characteristics

Primary Versus Secondary Carcinoma

A fundamental question in this review was whether the tumor in the second breast

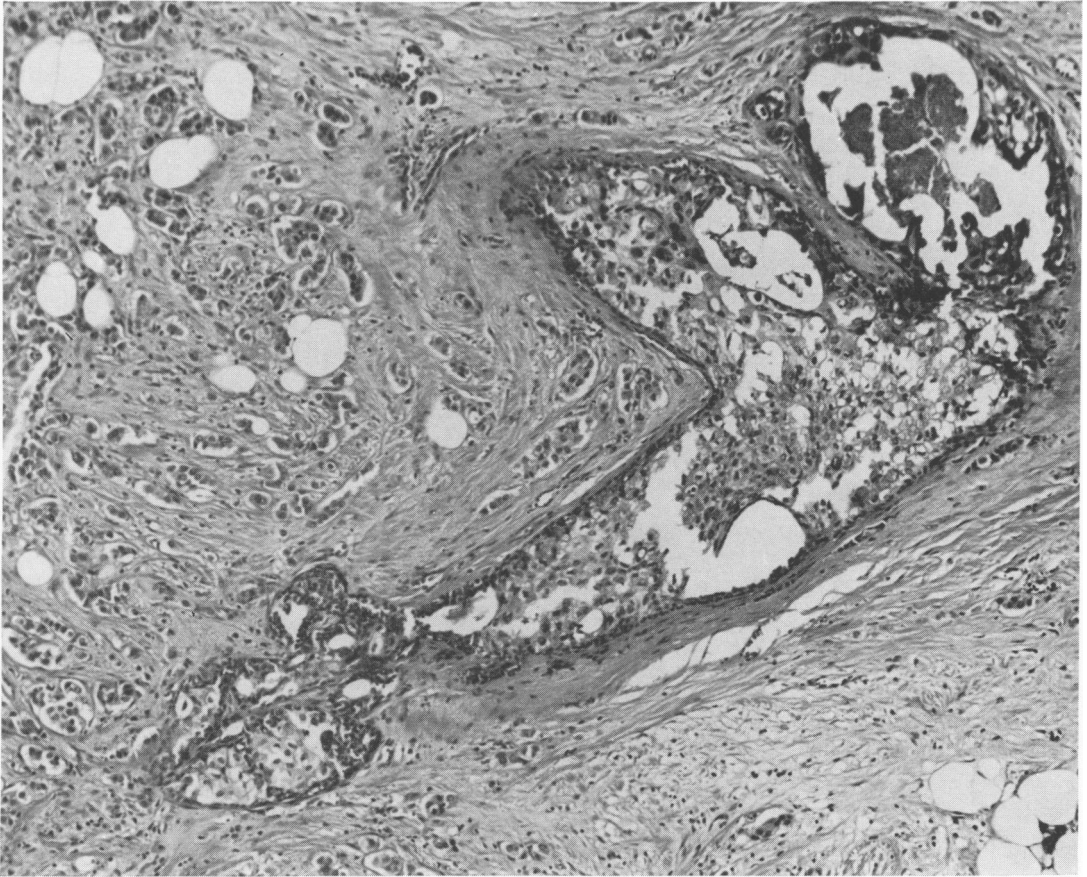


FIG. 2. Scirrhous carcinoma in "second" breast. Contiguous intraductal carcinoma (comedo pattern) on right ($\times 16$).

was a new primary or a metastatic lesion. The clinical criteria of Haagenson⁵ and the pathological criteria as reported by Robbins and Berg¹² were used in this analysis. The criteria are summarized in Tables 3 and 4. By these criteria, 30 cases, for whom an adequate pathologic review could be accomplished, had separate and independent primary tumors. The absolute criterion for this distinction is the demonstration of *in situ* carcinoma in the breast tissue contiguous to the invasive carcinoma. This was found in 59 of the breasts. The sixtieth case was a stromal sarcoma, obviously different from the contralateral carcinoma.

It is our belief that histological dissimilarity between two breast carcinomas is not

an adequate criterion for making this distinction. Figures 2, 3, and 4 show the type of *in situ* change which is necessary to label a breast carcinoma as primary.

TABLE 2. Fertility as Expressed by Percentage of Women Bearing \times Number of Children

	U. S. Population 16-44 Years— Year 1960	Our Sample
Childless	10	30
One child	14	27
Two-four children	64	43
Five + children	13	0

Table 2 shows fertility among bilateral breast cancer cases as compared to the United States population.

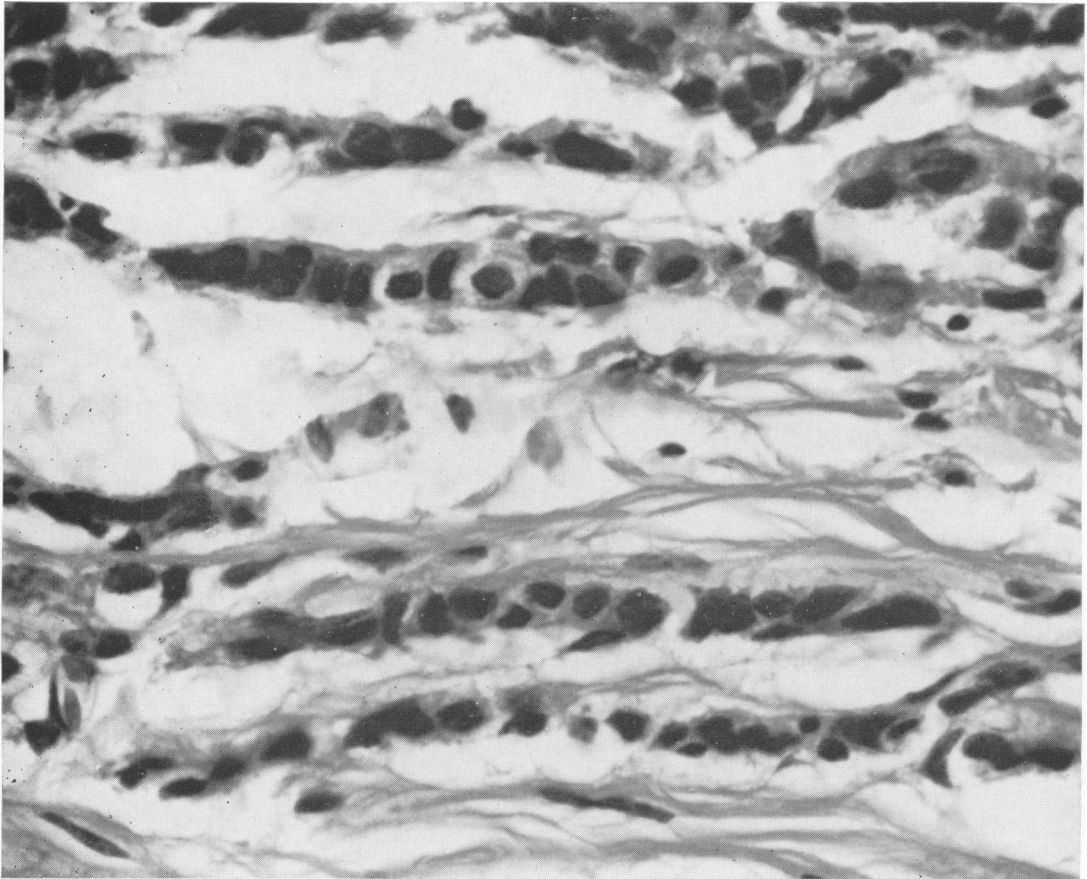


FIG. 3. Infiltrating lobular carcinoma in "second" breast. Typical "Indian File" Pattern ($\times 100$).

Histological Classification

Classification of the tumors in this series according to the scheme of McDivitt *et al.*¹⁰ is shown in Table 5. Four cases in which

TABLE 3. *Clinical Features of Metastatic Carcinomas vs. New Primaries in Second Breast*

	Metastatic	New Primary
Spread across midline of chest to second breast	Present	Absent
Number of lesions	Usually multiple	Solitary
Distant metastases	Present	Absent

Table 3 shows clinical features used to distinguish primary versus metastatic carcinomas in the second breast (after Haagensen).

only *in situ* carcinoma was present, one intraductal and three lobular, are excluded. One breast contained a stromal sarcoma. The remaining 55 breasts contained invasive breast cancer.

Comparison of the distribution of histologic types in these 55 breast specimens with the types found in a large series of unilateral breast carcinoma reported by McDivitt¹⁰ demonstrates an increased incidence of both lobular and tubular carcinoma in our specimens (Table 6). This increased incidence of lobular carcinoma is not unexpected since it has a propensity to occur in both breasts.

The unexpected finding was the high incidence of tubular carcinoma. This rare but

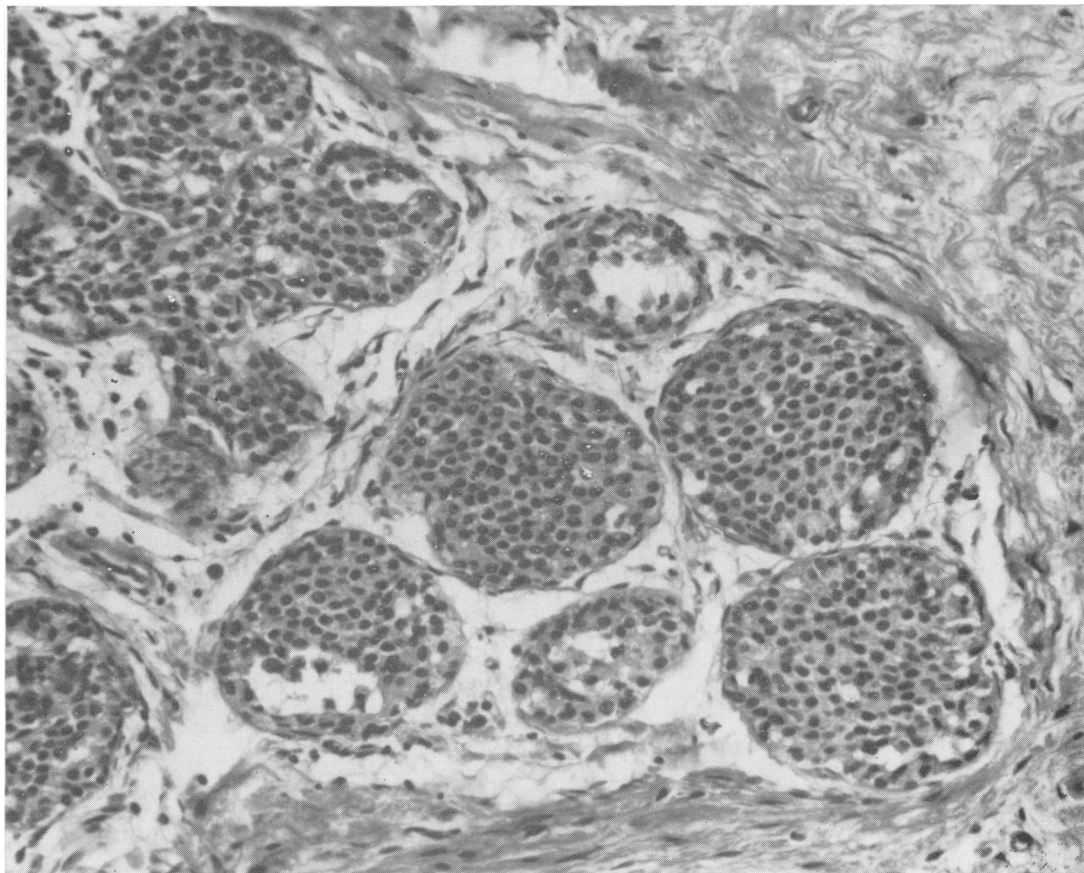


FIG. 4. Lobular carcinoma-*in-situ* present adjacent to invasive carcinoma illustrated in Fig. 3 ($\times 51$).

specific type of breast tumor is also known as well-differentiated or orderly carcinoma. It occurred in 9% of the breast specimens in this series. This incidence is to be compared with the series of McDivitt *et al.*¹⁰ who found it to occur in less than 1% of their specimens of unilateral breast carcinoma. Figures 5 and 6 show histological sections of this tumor, which may have a deceptively innocent appearance. The only series of tubular carcinoma known to us is that of Taylor and Norris.¹³ One of their 33 cases had bilateral synchronous tubular carcinoma, and six other patients subsequently developed carcinoma in the opposite breast 1 to 8 years after treatment of their initial primary tumors. It would appear that tu-

TABLE 4. *Pathological Features of Metastatic Carcinomas vs. New Primaries in Second Breast*

	Metastatic	New Primary
Location	In the fat surrounding the breast parenchyma	Within the breast parenchyma
Growth pattern Histology	Expansile Resembles the most malignant part of primary	Infiltrating Histologically dissimilar
Contiguous <i>in-situ</i> carcinoma	Absent	Present

Table 4 shows pathological features used to distinguish between primary and metastatic carcinoma in the second breast (after Robbins and Berg).

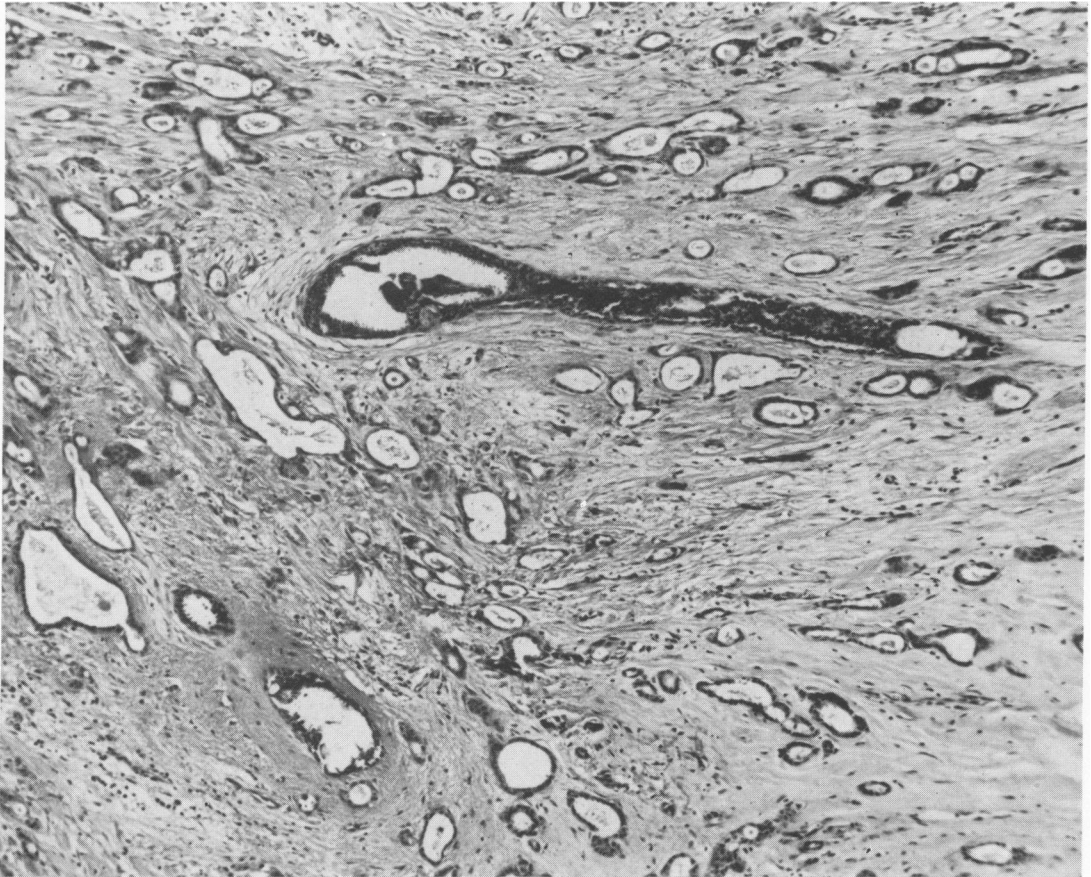


FIG. 5. Tubular carcinoma showing diffuse infiltration ($\times 20$).

bular carcinoma, like lobular carcinoma, may tend to be a bilateral disease.

Gross Multicentricity

This characteristic in which more than one separate and discrete primary malig-

nancies are found in a single breast occurred in five of the 55 invasive carcinomas in our series. Three were in one of the breasts of the synchronous cases, and two were in the second breast of the asynchronous group. Multicentricity is not an adequate criterion to prove metastatic involvement in the second breast. Both of the asynchronous cases with multicentricity demonstrated *in situ* carcinoma contiguous with the multiple carcinomas.

Robbins and Berg¹² found gross multicentricity a factor predisposing towards development of carcinoma in the second breast. This was not demonstrated in our series.

TABLE 5. Classification of Sixty Bilateral Breast Cancers

Intraductal	1	Metaplastic	1
Comedo	2	Stromal sarcoma	1
Scirrhus	36	Lobular- <i>in situ</i>	3
Medullary	1	Infiltrating lobular	9
Colloid	1	Tubular	5

Table 5 shows pathologic classification of 60 bilateral breast cancers in our series using criteria of McDivitt *et al.*

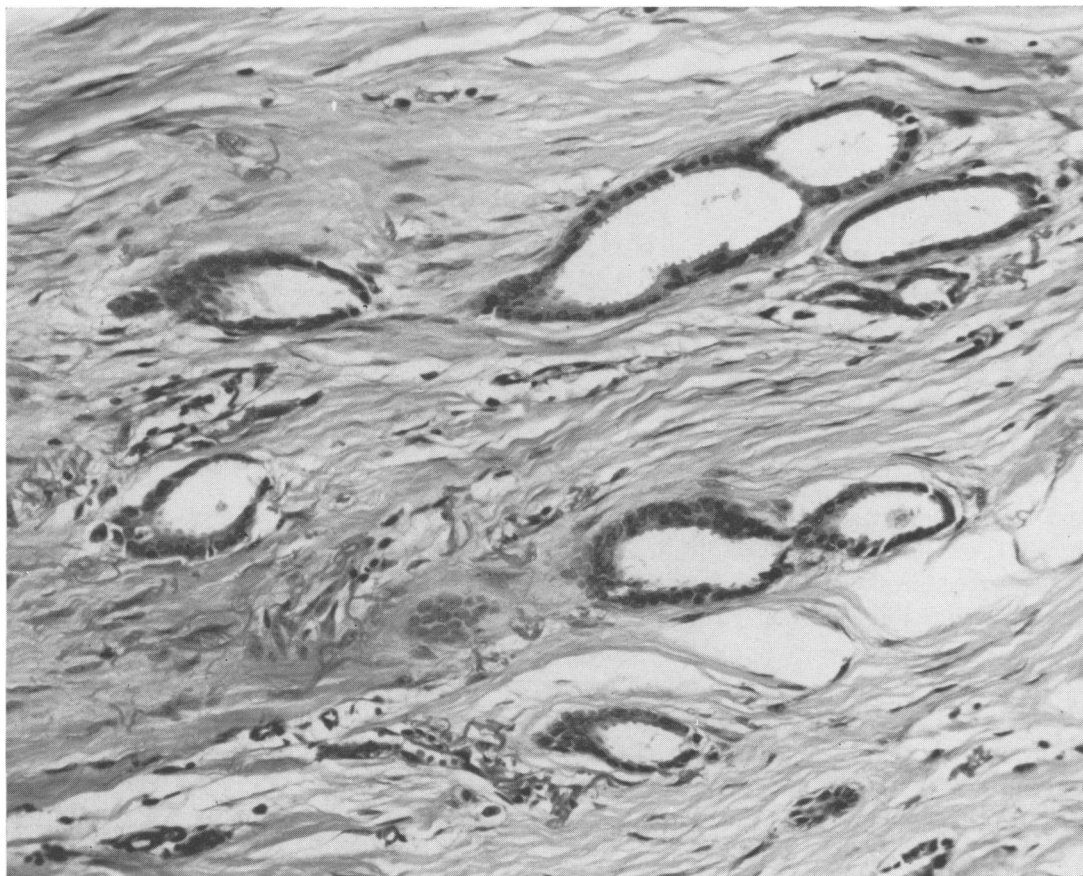


FIG. 6. Tubular carcinoma showing deceptively innocent histologic appearance ($\times 51$).

Other Parameters

No significant correlations were noted with regard to the size of the carcinomas nor the presence or absence of associated cystic disease. No correlations could be made with grade of tumor. None of the patients had Paget's disease of the nipple.

Blood vessel invasion was noted in four of the 55 breast specimens containing invasive carcinoma. Two of four patients died of metastatic disease. The other two have been followed for less than 1 year. Neither has shown evidence of metastatic disease.

Treatment and Survival

Surgical treatment used is shown in Table 7. It is remarkably uniform, as radi-

TABLE 6. Incidence of Histological Type of Invasive (55) Bilateral Breast Carcinoma as Compared with Memorial Hospital Series of Breast Carcinomas

Type	Memorial Series	Authors Series	
		Expected No.	Actual No.
Comedo	4.6%	2	2
Scirrhous	78.1%	43	36
Medullary	4.3%	2	1
Colloid	2.6%	1	1
Metaplastic	1.0%	0.5	1
Invasive lobular	8.7%	5	9
Tubular	1.0%	0.5	5

Table 6 shows comparison of incidence of various types of breast carcinoma between large series of unilateral and our series of bilateral cases.

TABLE 7. *Miscellaneous Information*

Surgical treatment	
Radical	78%
Radical	
Radical	
Simple	10%
Simple	
Simple	
Simple	7%
Simple	
Other	5%

Table 7 presents the percentage of patients receiving different modes of surgical therapy to their first and second primaries.

cal mastectomy was performed bilaterally in 78% of our cases. Our indications for lesser procedures were enumerated in our previous communications.⁴

The survivals were computed by using the ratio of possible survivals to patients dying up to stated years of clinical follow-up (Table 8). Our crude (uncorrected for age) survival is 80% at 5 years, 50% at 10 years, and 33% at 15 years. The number of patients was deemed too small to compute meaningful survivals if the group were subdivided according to the stage of disease. The 5-year survival among our patients with synchronous disease is 90%; however, only one patient survived 10 years.

Summary

A series of 50 patients with bilateral breast cancer treated by our group practice is presented. Epidemiological review reveals these patients to be younger, less fertile, and having strong family history of breast cancer. The pathologic evaluation revealed all of the second breast tumors studied to be primary neoplasms. The approach to treatment was based on the assumption that the contralateral carcinoma was a separate and distinct primary tumor. The reported survivorship seems to justify this approach to treatment. Another salient

TABLE 8. *Per cent Survivorship to Stated Years*

Survival in Years	Bilateral from First Surgery	Bilateral from Second Surgery	Synchron- ous
	Cases	50	
5	85	50	90
10	50	44	20
15	33	8	0
20	20	0	0

Table 8 shows percentage of survival of patients from onset of their disease compared with survival from the time of diagnosis of second malignancy, and also, with survivals in the synchronous tumor group.

feature of this group is an unexpectedly high incidence of tubular carcinoma.

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